QC TEST REQUESTS

Air/Surface Sample Location	**Description**	**Results**		
		Bacteria CFU	*Mold CFU*	*Total CFU*

Date of Sampling: Media Lot#: Exp Date:
Sampler Mfg/Model: Calibration Due Date:

Quality Control: Date:

Reviewed By: Date:

ORIGINAL

RANDOM AIR/SURFACE SAMPLING - ATTACHMENT 4

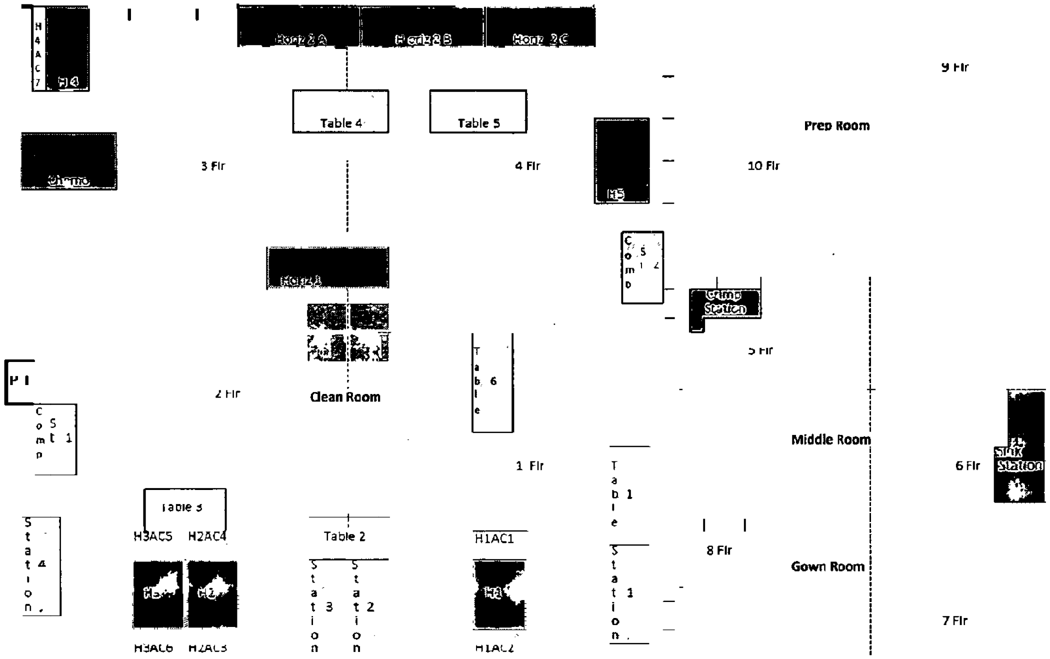
Air/Surface Sample Location	Description	Results		
		Bacteria CFU	***Mold CFU***	***Total CFU***

Date of Sampling: Media Lot#: Exp Date:
Sampler Mfg/Model: Calibration Due Date:

Quality Control: Date:

Reviewed By: Date:

ORIGINAL



CLEAN ROOM SURFACE

Attachment 6

Two random walls
clean room
middle room
gown room
prep room

Two IPA bottles once a month

Two random bins/misc samples
clean room
middle room
prep room
gown room

CLEAN ROOM SURFACE SAMPLING

Page 2 of 2

		Results			
Sample Location	Description	Bacteria CFU	Mold CFU	Total CFU	**Alert/Action**
SINK STATION	Sink Station				☐ **Alert** ☐ **Action**
CRIMP STATION	Crimp Station				☐ **Alert** ☐ **Action**
WALL CR 1	Clean Room Wall 1				☐ **Alert** ☐ **Action**
WALL CR 2	Clean Room Wall 2				☐ **Alert** ☐ **Action**
WALL MR 1	Middle Room Wall 1				☐ **Alert** ☐ **Action**
WALL MR 2	Middle Room Wall 2				☐ **Alert** ☐ **Action**
WALL GR 1	Gown Room Wall 1				☐ **Alert** ☐ **Action**
WALL GR 2	Gown Room Wall 2				☐ **Alert** ☐ **Action**
WALL PREP 1	Prep Room 1				☐ **Alert** ☐ **Action**
WALL PREP 2	Prep Room 2				☐ **Alert** ☐ **Action**
1FLR	1 Floor (near hood 1)				☐ **Alert** ☐ **Action**
2FLR	2 Floor (near hood 3)				☐ **Alert** ☐ **Action**
3FLR	3 Floor (near horizontal hoods)				☐ **Alert** ☐ **Action**
4FLR	4 Floor (near hood 5)				☐ **Alert** ☐ **Action**
5FLR	5 Floor (near crimp bench)				☐ **Alert** ☐ **Action**
6FLR	6 Floor (near sink)				☐ **Alert** ☐ **Action**
7FLR	7 Floor (gown room - entrance)				☐ **Alert** ☐ **Action**
8FLR	8 Floor (gown room - near hooks)				☐ **Alert** ☐ **Action**
9FLR	9 Floor (prep room - near entrance)				☐ **Alert** ☐ **Action**
10FLR	10 Floor (prep room - near big Pass Thru				☐ **Alert** ☐ **Action**
RANDOM/BINCR1	Clean room bin or random surface				☐ **Alert** ☐ **Action**
RANDOM/BINCR2	Clean room bin or random surface				☐ **Alert** ☐ **Action**
RANDOM/BINMR1	Middle room bin or random surface				☐ **Alert** ☐ **Action**
RANDOM/BINMR2	Middle room bin or random surface				☐ **Alert** ☐ **Action**
RANDOM/BINPREP1	Prep room bin or random surface				☐ **Alert** ☐ **Action**
RANDOM/BINPREP2	Prep room bin or random surface				☐ **Alert** ☐ **Action**
SINK STATION	Sink Station				☐ **Alert** ☐ **Action**
CRIMP STATION	Crimp Station				☐ **Alert** ☐ **Action**
1IPA	Alcohol				☐ **Alert** ☐ **Action**
2IPA	Alcohol				☐ **Alert** ☐ **Action**

Quality Control: Date:

Reviewed By: Date:

CLEAN ROOM SURFACE SAMPLING

		Results			
Sample Location	Description	Bacteria CFU	Mold CFU	Total CFU	**Alert/Action**
H1	Hood 1				☐ **Alert** ☐ **Action**
H1AC1	Hood 1 Antechamber (Right Side)				☐ **Alert** ☐ **Action**
H1AC2	Hood 1 Antechamber (Left Side)				☐ **Alert** ☐ **Action**
H2	Hood 2				☐ **Alert** ☐ **Action**
H2AC3	Hood 2 Antechamber (Right Side)				☐ **Alert** ☐ **Action**
H2AC4	Hood 2 Antechamber (Left Side)				☐ **Alert** ☐ **Action**
H3	Hood 3				☐ **Alert** ☐ **Action**
H3AC5	Hood 3 Antechamber (Right Side)				☐ **Alert** ☐ **Action**
H3AC6	Hood 3 Antechamber (Left Side)				☐ **Alert** ☐ **Action**
H4	Hood 4				☐ **Alert** ☐ **Action**
H4AC7	Hood 4 Antechamber				☐ **Alert** ☐ **Action**
H5	Hood 5				☐ **Alert** ☐ **Action**
CHEMO	Chemo Hood				☐ **Alert** ☐ **Action**
HORIZ 1	Horizontal 1				☐ **Alert** ☐ **Action**
HORIZ 2A	Horizontal 2A				☐ **Alert** ☐ **Action**
HORIZ 2B	Horizontal 2B				☐ **Alert** ☐ **Action**
HORIZ 2C	Horizontal 2C				☐ **Alert** ☐ **Action**
STATION 1	Station 1				☐ **Alert** ☐ **Action**
STATION 2	Station 2				☐ **Alert** ☐ **Action**
STATION 3	Station 3				☐ **Alert** ☐ **Action**
STATION 4	Station 4				☐ **Alert** ☐ **Action**
PASS THRU	Pass Thru				☐ **Alert** ☐ **Action**
TABLE 1	Table 1				☐ **Alert** ☐ **Action**
TABLE 2	Table 2				☐ **Alert** ☐ **Action**
TABLE 3	Table 3				☐ **Alert** ☐ **Action**
TABLE 4	Table 4				☐ **Alert** ☐ **Action**
TABLE 5	Table 5				☐ **Alert** ☐ **Action**
TABLE 6	Table 6				☐ **Alert** ☐ **Action**
COMP. ST. 1	Computer Station 1				☐ **Alert** ☐ **Action**
COMP. ST. 2	Computer Station 2				☐ **Alert** ☐ **Action**

Quality Control: Date:
Reviewed By: Date: [redacted]

CLEAN ROOM SURFACE SAMPLING - ATTACHMENT 2

(Page 2 of 2)

Sample Location	Description	Results			Alert/ Action
		Bacteria CFU	*Mold CFU*	*Total CFU*	
SinkS	Sink in Crimp Room				☐Al ☐Ac
CrimpS	Crimping Bench				☐Al ☐Ac
1RBS	Random Bin				☐Al ☐Ac
2RBS	Random Bin				☐Al ☐Ac
1GRFS	Gown Room – Near Hall				☐Al ☐Ac
2GRFS	Gown Room – Near Clean room				☐Al ☐Ac
1PFS	Prep Room – Near Incubator				☐Al ☐Ac
2PFS	Prep Room – Near Warehouse				☐Al ☐Ac
1FLRS	Clean Room Floor				☐Al ☐Ac
2FLRS	Clean Room Floor				☐Al ☐Ac
3FLRS	Clean Room Floor				☐Al ☐Ac
4FLRS	Clean Room Floor				☐Al ☐Ac
5FLRS	Clean Room Floor				☐Al ☐Ac
6FLRS	Clean Room Floor				☐Al ☐Ac
1IPAS	Isopropyl Alcohol				☐Al ☐Ac
2IPAS	Isopropyl Alcohol				☐Al ☐Ac

Alert	**Action**
1 CFU ISO 4 (class 10) Glove box, Antechambers	2+ CFU
3 CFU ISO 6 (class 1,000) Main Clean room	5+ CFU
5 CFU ISO 7 (class 10,000) Gown room, Crimp room	7+ CFU
8 CFU ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling: Media Lot: Exp Date:

Quality Control: Date:
Reviewed By: Date:

ORIGINAL
uwl
07-22-08

CLEAN ROOM SURFACE SAMPLING - ATTACHMENT 2

(Page 1 of 2)

Sample Location	Description	Results			Alert/ Action
		Bacteria CFU	*Mold CFU*	*Total CFU*	
H51S	Hood 1				☐Al ☐Ac
H52S	Hood 2				☐Al ☐Ac
H53S	Hood 3				☐Al ☐Ac
H54S	Hood 4				☐Al ☐Ac
H55S	Hood 5				☐Al ☐Ac
1ACS	Hood 1 Antechamber (Right Side)				☐Al ☐Ac
2ACS	Hood 1 Antechamber (Left Side)				☐Al ☐Ac
3ACS	Hood 2 Antechamber (Right Side)				☐Al ☐Ac
4ACS	Hood 2 Antechamber (Left Side)				☐Al ☐Ac
5ACS	Hood 3 Antechamber (Left Side)				☐Al ☐Ac
6ACS	Hood 3 Antechamber (Right Side)				☐Al ☐Ac
7ACS	Hood 4 Antechamber				☐Al ☐Ac
ChemoS	Chemo Hood				☐Al ☐Ac
HorizS	Horizontal Hood				☐Al ☐Ac
H50TS	Table 1				☐Al ☐Ac
H51TS	Table 2				☐Al ☐Ac
H52TS	Table 3				☐Al ☐Ac
H53TS	Table 4				☐Al ☐Ac
H54TS	Table 5				☐Al ☐Ac
1PTS	Pass - thru				☐Al ☐Ac
2PTS	Pass - thru				☐Al ☐Ac
3PTS	Pass - thru				☐Al ☐Ac

ORIGINAL
04-22-08

RANDOM AIR/SURFACE SAMPLING - ATTACHMENT 4

Air/Surface Sample Location	Description	Results		
		Bacteria CFU	***Mold CFU***	***Total CFU***

Date of Sampling:
Media Lot#:
Exp Date:
Sampler Mfg/Model:
Calibration Due Date:

Quality Control:
Date:

Reviewed By:
Date:

ORIGINAL
AUK 0922-08

CLEAN ROOM SURFACE SAMPLING

Attachment 4

Page 2 of 2

Sample Location	Description	Results Bacteria CFU	 Mold CFU	 Total CFU	Alert/Action
SINK STATION	Sink Station				☐ Alert ☐ Action
CRIMP STATION	Crimp Station				☐ Alert ☐ Action
WALL CR 1	Clean Room Wall 1				☐ Alert ☐ Action
WALL CR 2	Clean Room Wall 2				☐ Alert ☐ Action
WALL MR 1	Middle Room Wall 1				☐ Alert ☐ Action
WALL MR 2	Middle Room Wall 2				☐ Alert ☐ Action
WALL GR 1	Gown Room Wall 1				☐ Alert ☐ Action
WALL GR 2	Gown Room Wall 2				☐ Alert ☐ Action
WALL PREP 1	Prep Room 1				☐ Alert ☐ Action
WALL PREP 2	Prep Room 2				☐ Alert ☐ Action
1FLR	1 Floor (near hood 1)				☐ Alert ☐ Action
2FLR	2 Floor (near hood 3)				☐ Alert ☐ Action
3FLR	3 Floor (near horizontal hoods)				☐ Alert ☐ Action
4FLR	4 Floor (near hood 5)				☐ Alert ☐ Action
5FLR	5 Floor (near crimp bench)				☐ Alert ☐ Action
6FLR	6 Floor (near sink)				☐ Alert ☐ Action
7FLR	7 Floor (gown room - entrance)				☐ Alert ☐ Action
8FLR	8 Floor (gown room - near hooks)				☐ Alert ☐ Action
9FLR	9 Floor (prep room - near entrance)				☐ Alert ☐ Action
10FLR	10 Floor (prep room - near big Pass Thru				☐ Alert ☐ Action
RANDOM/BINCR1	1 Clean room bin or random surface				☐ Alert ☐ Action
RANDOM/BINCR2	2 Clean room bin or random surface				☐ Alert ☐ Action
RANDOM/BINMR1	1 Middle room bin or random surface				☐ Alert ☐ Action
RANDOM/BINMR2	2 Middle room bin or random surface				☐ Alert ☐ Action
RANDOM/BINPREP1	1 Prep room bin or random surface				☐ Alert ☐ Action
RANDOM/BINPREP2	2 Prep room bin or random surface				☐ Alert ☐ Action
SINK STATION	Sink Station				☐ Alert ☐ Action
CRIMP STATION	Crimp Station				☐ Alert ☐ Action
1IPA	Alcohol				☐ Alert ☐ Action
2IPA	Alcohol				☐ Alert ☐ Action

Quality Control: Date:
Reviewed By: Date:

TITLE: ENVIRONMENTAL MONITORING OF CLEAN ROOM AREAS

SOP NUMBER: 3.030	**VERSION NUMBER: 3.0**
DATE EFFECTIVE:	**DEPARTMENT: ADMIXING**

Written By:	Signature	Date:
Quality Approval:	Signature	Date:
Compliance Approval:	Signature	Date:

1.0 PURPOSE

1.1 The purpose of this procedure is to establish the requirements for the Environmental Monitoring (EM) program within the Clean Room facility. The program is designed to monitor viable and non-viable air quality, the viable load on surfaces, and the viable load on compounders working within the hoods.

2.0 SCOPE

2.1 This procedure applies to the Ameridose clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This SOP applies to all personnel who perform any function within the Environmental Monitoring program.

3.0 RESPONSIBILITY

3.1 Personnel following this SOP are responsible for completing all required training prior to performing any tasks in this procedure.

3.2 Quality Assurance shall perform all Environmental and Personnel Monitoring.

3.3 The Quality Assurance Director shall manage this procedure and ensure that personnel responsible for Environmental and Personnel Monitoring of the Clean Room Areas comply with this procedure.

3.4 The Quality Assurance Director shall report deviations, Alert/Action excursions, and trending, as appropriate, to the Quality Assurance Committee.

3.5 The Quality Assurance Committee shall oversee this procedure and review deviations, Alert/Action excursions, and trending as appropriate

4.0 REFERENCES

4.1 USP <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644 "Clean Rooms and Associated Controlled Environments"

4.4 SOP 1.030 " Deviation-OOS"

4.5 SOP 9.090 "Required Garb for Clean Room Facility Access

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Surface Contact Plate – Agar plate used to sample surfaces for microorganisms by direct application. The agar contains neutralizers to inactivate residual disinfectants.

5.3 ISO Classifications

- 5.3.1 ISO Class 5 is equivalent to Class 100
- 5.3.2 ISO Class 6 is equivalent to Class 1,000
- 5.3.3 ISO Class 7 is equivalent to Class 10,000
- 5.3.4 ISO Class 8 is equivalent to Class 100,000

5.4 Alert Level – Signals a potential drift from normal operating conditions when normal levels of viable/non-viable particulate in a controlled environment are exceeded. Alert level does not require investigation.

5.5 Action Level – Signals a potential drift from normal operating conditions when normal levels of viable/non-viable particulate in a controlled environment are exceeded. Action level requires an investigation and corresponding corrective action.

5.6 TSA – Tripticase Soy Agar

5.7 At-rest – Condition where the installation is complete with equipment installed and operating in a manner agreed upon by customer and supplier but with no personnel present.

5.8 Operational – Condition where the installation is functioning in the specified manner, with the specified number of personnel present and working in the manner agreed upon.

5.9 Requalification – Testing performed after a disruption to the area/equipment in order to demonstrate continued performance below Alert/Action levels.

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled weekly for each compounder working in a hood.

6.2 Surface sampling shall be performed weekly on a rotating schedule.

6.3 Viable air sampling shall be performed every 2 weeks on a rotating schedule.

6.4 Non-viable air sampling shall be performed at least every six months.

6.5 Environmental and Personnel Monitoring data shall be trended on a quarterly basis and reviewed by the Quality Assurance Committee.

7.0 EQUIPMENT & SUPPLIES

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 Calibrated viable air sampler

7.4 Appropriate equipment operating manuals

7.5 Sterile compounding garb and disinfectants as described in SOP 9.090

8.0 ATTACHMENTS

8.1 Attachment 1 – Alert/Action Levels

8.2 Attachment 2 - Media Log

8.3 Attachment 3 – Clean Room 1 - Viable Air Sampling Form

8.4 Attachment 4 – Clean Room 1 - Viable Air Sampling Map

8.5 Attachment 5 – Clean Room 2 - Viable Air Sampling Form

8.6 Attachment 6 – Clean Room 2 - Viable Air Sampling Map

8.7 Attachment 7 – Clean Room 1 - Surface Sampling Form

8.8 Attachment 8 – Clean Room 1 - Surface Sampling Map

8.9 Attachment 9 – Clean Room 2 - Surface Sampling Form

8.10 Attachment 10 – Clean Room 2 - Surface Sampling Map

8.11 Attachment 11 - Personnel Sampling Form

8.12 Attachment 12 - Additional Sample Form

8.13 Attachment 13 – Alert/Action Log

8.14 Attachment 14 – Alert Follow-up Form

9.0 GENERAL INFORMATION

9.1 Environmental Monitoring should flow from "clean" areas to "dirty" areas.

9.2 Personnel who perform sampling shall be gowned appropriately for the area as described in SOP 9.090.

9.3 During sampling of the clean areas, the sampler should sanitize hands with 70% IPA routinely and allow to dry. Sanitize hands more frequently if hands come in contact with dirty areas such as floors, chairs, doors, etc.

9.4 Sample sites shall be selected based on proximity to critical processing or high risk areas as well as proximity to high-traffic areas.

10.0 PROCEDURE

10.1 Media Receipt

10.1.1 Obtain commercially prepared TSA contact plates and the corresponding manufacturer's Certificate of Analysis (CoA)

10.1.2 Verify that the CoA documents that growth promotion testing was successfully completed and that the information on the CoA corresponds to the media shipment.

10.1.2.1 Document the date and quantity received on the CoA. Initial and date the CoA.

10.1.2.2 If documentation is not provided, set aside the media and do not use until appropriate certification is received.

10.1.3 Visually inspect the media packaging to ensure that it is not damaged.

10.1.3.1 Do not use damaged media. Return or dispose of the material as appropriate.

10.1.4 Document receipt of the media on Attachment 2. Complete all applicable sections.

10.1.5 Store Attachment 2 and associated CoAs in a dedicated binder.

10.1.6 Store the media according to the manufacturer's recommendation (usually 2°C-8°C) in a monitored refrigerator.

10.2 Preparation for sampling

10.2.1 Obtain the appropriate quantity and type of media from storage.

10.2.2 Remove the outer packaging and inspect. Discard any damaged or contaminated media.

10.2.3 Verify media is within expiration date and record the lot number and expiration date on the appropriate attachment.

10.2.4 Verify that the sampling equipment is within calibration and document the make, model, serial number and calibration due date on the appropriate attachment.

10.2.5 Sanitize the exterior of the materials and equipment per SOP 9.090 prior to entry into the clean room facility.

10.2.6 Don all appropriate clean room garb and gloves as per SOP 9.090

10.3 Non-Viable Air Sampling

10.3.1 Non-viable air sampling shall be performed every 6 months along with Room/Hood Certification.

10.3.2 Sampling shall be performed by an approved vendor using calibrated equipment.

10.3.3 Forward all documentation to the Quality Assurance for review.

10.3.4 File all completed documents in the designated binder.

10.4 Viable Air Sampling

10.4.1 The sample locations listed on Attachment 3 and 5 for Clean Rooms 1 and 2 shall be sampled every 2 weeks. Refer to Attachment 4 and 6 for sample location proximity.

10.4.2 Document all data on the appropriate Attachment.

10.4.3 Set up the air sampler according to the manufacturer's instructions.

10.4.4 Sanitize the exterior of the sampler prior to use with a low-lint wipe saturated with 70% IPA.

10.4.5 If the sampler is being moved from a dirty to clean location during sampling, repeat exterior sanitization.

10.4.6 Ensure the sampler is programmed with the following parameters:

Sample time	Air Volume/Minute	Total Air Volume
5.5 Minutes	180 liters	1000 liters (35ft^3)

10.4.7 Document the status of the area/room on the appropriate Attachment.

10.4.8 Remove the contact plates from the inner packaging wrapper. Ensure that the contact plate cover remains on.

10.4.9 Aseptically remove the outer protective cap from the sampler and unscrew the aspirating head.

10.4.10 Secure the plate between the metal prongs. Once secure, remove the contact plate cover and immediately replace the aspirating head and screw on tightly.

Note: Do not touch the agar surface (If agar is touched, discard the contact plate.

10.4.11 Place the air sampler in the desired location at cart or bench-top height. Orient the air sampler a vertical position facing the ceiling and turn on. **Do not stand over the sampler while in operation.**

Note: Do not sample hoods when compounders are in the process of performing an aseptic manipulation. Wait until the manipulation is complete prior to sampling.

10.4.12 The air sampler will automatically turn off at the conclusion of the sampling period.

10.4.13 Aseptically replace the contact plate cover and remove the contact plate from the sampler.

10.4.14 Seal the contact plate with parafilm.

- 10.4.14.1 Inspect the contact plate to ensure that impingement marks are present.
- 10.4.14.2 If impingement marks are not present, the sample is invalid and shall be repeated with a new contact plate.

10.4.15 Record the site location on the base of the plate and initial and date. Do not record any information on the cover of the plate.

10.4.16 Invert the samples and incubate for as follows

- 2 days (48 hours) at 30-35°C
- 5 additional days (120 hours) 20-25°C.

Note: Samples may be shipped to a contract lab for incubation and analysis.

Note: If 2nd day of incubation falls on a non-business day, then the plates shall be transferred to the next temperature on the next business day. They shall be incubated at that temperature for the remainder of the 7 days. Do not exceed 7 days of incubation.

10.4.17 Document start and stop times on the appropriate Attachment.

Note: Samples must be incubated within 2 hours of sampling.

10.5 Surface Sampling

10.5.1 The sample locations listed on Attachment 7 and 9 for Clean Rooms 1 and 2 shall be sampled weekly. Refer to Attachment 8 and 10 for sample location proximity.

10.5.2 Document all data on the appropriate Attachment. Record the status of the hood/area.

10.5.3 Remove the contact plates from the inner packaging wrapper. Ensure that the contact plate cover remains on.

Note: Do not sample hoods when compounders are in the process of performing an aseptic manipulation. Wait until the manipulation is complete prior to sampling.

10.5.4 Ensure that surfaces are dry before sampling.

10.5.5 Aseptically remove the contact plate cover.

Note: Do not touch the agar surface (If agar is touched, discard the plate).

10.5.6 Invert the plate and gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface.

10.5.7 Replace the cover and seal the plate with parafilm.

10.5.8 Record the site location on the base of the plate and initial and date. Do not record any information on the cover of the plate.

10.5.9 Wipe the sample site with a wipe saturated with IPA to remove residual agar.

10.5.10 Invert the samples and incubate for as follows

- 2 days (48 hours) at 30-35°C
- 5 additional days (120 hours) 20-25°C.

Note: Samples may be shipped to a contract lab for incubation and analysis.

Not : If 2nd day of incubation falls on a non-business day, then the plates shall be transferred to the next temperature on the next business day. They shall be incubated at that temperature for the remainder of the 7 days. Do not exceed 7 days of incubation.

10.5.11 Document start and stop times on the appropriate Attachment.

Note: Samples must be incubated within 2 hours of sampling.

10.6 Personnel Monitoring

10.6.1 Sample all compounders working directly in the hoods on each business day.

10.6.2 Document all data on Attachment 11.

Note: Do not sample compounders who are in the process of performing an aseptic manipulation. Wait until the manipulation is complete prior to sampling.

10.6.3 Record the compounder's name, the hand sampled and the hood in which he/she is working on Attachment 11.

Note: Compounder shall not sanitize hands or change gloves immediately prior to being sampled.

10.6.4 Aseptically place the agar plate in hood in which the compounder is working, agar side up.

10.6.5 Open the cover of the contact plate and have the compounder roll each gloved finger (of the dominant hand) one at a time on the plate, making certain not to re-touch areas.

10.6.6 Replace the cover and seal the plate with tape/parafilm.

10.6.7 Record the compounder's name on the base of the plate and initial and date. Do not record any information on the cover of the plate.

10.6.8 The compounder shall replace gloves and re-sanitize hands accordingly prior to resuming operations in the hood.

10.6.9 Invert the samples and incubate for as follows

- 2 days (48 hours) at 30-35ºC
- 5 additional days (120 hours) 20-25ºC.

Note: Samples may be shipped to a contract lab for incubation and analysis.

Note: If 2nd day of incubation falls on a non-business day, then the plates shall be transferred to the next temperature on the next business day. They shall be incubated at that temperature for the remainder of the 7 days. Do not exceed 7 days of incubation.

10.6.10 Document start and stop times on Attachment 11.

Note: Samples must be incubated within 2 hours of sampling.

10.7 Non-Routine Samples

10.7.1 Non-routine samples that are not listed on the Viable and Surface Sampling Forms may be taken at a desired location.

10.7.2 Take the sample according to the appropriate air or surface sampling procedure above.

10.7.3 Document the sample location, sampling, and results on Attachment 12.

10.7.4 Non-routine samples are investigational and shall not be compared to alert/action values. Do not generate an alert or action as described in 10.9 for non-routine samples.

10.8 Reporting Results

10.8.1 Remove samples from the incubator. Record stop times on the appropriate attachment.

10.8.2 Count all colonies on the plate and document results for each category below.

- Bacteria
- Mold (Count or indicate presence)
- Total Counts of Bacteria and Mold combined

Note: 200 colonies per plate is the maximum number of colonies that can be counted. If colonies per plate exceed 200 CFU, report the result as "Too numerous to count" (TNTC).

10.8.3 Calculate the level of viable airborne particulates as CFU per cubic foot.

Calculate the Total CFU/ft^3

$$\frac{\text{Total CFU per contact plate}}{35\text{ft}^3 \text{ of air sampled}} = \text{Total CFU/ft}^3$$

10.8.4 Count the level of surface viables (surface or personnel) as CFU/plate.

10.8.5 Record results on the appropriate attachment.

10.8.6 Compare results with corresponding Alert/Action on Attachment 1.

10.8.7 Forward completed Attachment to the Quality Assurance Director or designee for review.

10.8.8 File all completed documents in the designated binder.

10.9 Generation of Alert and Action Limits

10.9.1 Alert levels shall be derived from historical data. When historical data is not available, alert values may be set as a percentage of Action Level values.

10.9.2 Action levels shall be derived based on functionality/utilization of Clean Room areas, historical data and/or compendial guidelines.

10.9.3 Alert/Action levels shall be evaluated on an annual basis (as part of the trending report in section 10.11) to ensure that the levels are still applicable to the environment.

10.9.4 In the event that a new hood or clean room is put in service, Alert/Action levels shall be set using the levels for similar equipment/areas until sufficient historical data can be obtained and evaluated.

10.10 Alert/Action Excursion

10.10.1 When a sample exceeds the specified Alert or Action level, Quality Assurance shall assign a Tracking number and complete the appropriate sections on Attachment 8.

10.10.1.1 The format of the Tracking # shall be 5 digits, consisting of a 2-digit designation for the year followed by a 3 digit sequential number beginning at 001. The sequential number shall reset at the start of each year.

For example

The Tracking # for the 3rd excursion in 2007 shall be **"07-003"**

10.10.2 For Alert Level excursion, complete Attachment 9 to document follow up activities to ensure that the area/hood/compounder has returned to a state of control.

10.10.2.1 Clean the impacted area per applicable SOPs. Routine cleaning that was performed subsequent to the date on which the excursion occurred may satisfy the re-cleaning requirement.

10.10.2.2 Resample the impacted location per the applicable sections of this procedure for 1 day subsequent to re-cleaning. Routine sampling may satisfy re-sampling requirements.

Note: Investigation and/or further corrective action may be performed for individual Alert level excursions at the discretion of management. Proceed as described below and document rationale for the investigation.

10.10.3 For Action level excursions or multiple/re-occurring alert level excursions that require further investigation, complete an OOS Investigation per SOP 1.030.

10.10.4 If corrective actions are performed (other than routine cleaning and re-sampling), the area/compounder shall be requalified as described in Section 10.10. If all samples are within limits, the corrective action can be considered successful and the investigation closed. If any sample fails, additional investigation is required.

10.11 Requalification

10.11.1 Perform requalification sampling according to the applicable sections above for 1 day when the following events occur.

- Completion of a remedial action to correct and out-of compliance conditions.
- A significant change in the operational use of the hood/room.
- A significant interruption of air movement or an event which has potential for introducing large-scale contamination, for example air handler shut down, construction activities, large spills, introduction of new large-scale equipment, etc.
- Additional requalification sampling can occur at the discretion of Quality Assurance.

10.11.2 Requalification sampling will be evaluated against the defined Alert/Action levels.

10.12 Trending

10.12.1 Enter all environmental and personnel monitoring data into a spreadsheet to facilitate trending.

10.12.2 Trend the data using the following categories:

- Personnel Samples
- Hood Surface Samples
- Room Surface Samples/Room Air Samples

10.12.3 On a quarterly basis generate a report containing the following sections at a minimum. Trending shall evaluate a rolling 15 month data set to capture comparison of seasonal variance.

- List of all Alert/Actions
- Summary of all investigations and corrective actions
- Graphical depiction of all data
- Discussion of trends

10.12.4 Any trends identified shall be investigated and have corrective actions in place, as necessary.

10.12.5 The report shall be reviewed by the Quality Assurance Committee and signed by the following:

- Compliance Officer
- Director of Quality
- Director of Operations
- Director of Pharmacy

11.0 HISTORY

Version Number	Description of Change	Change Request Number
1.0	New SOP.	N/A
2.0	• Update Alert and Action Levels. Action Levels set at USP Clean Room Requirements. Alert Levels set at 50-70% of Action Levels. • Revise bi-phasic incubation requirements to reflect longer incubation time and more appropriate order of incubation temperatures. • Updated format and section to improve flow of SOP. • Changed frequency of viable air sampling to every 2 weeks. • Changed frequency of personnel monitoring to weekly. • Increased level of detail in procedure to improve clarity. • Included quarterly trending. • Updated procedure for tracking and responding to alerts/actions. • Added a section on requalification of clean Room Areas.	CR07008
3.0	• Adjusted Attachment for Alert Follow Up to remove redundant information • Minor wording changes for clarification of procedures • Added in sampling for Clean Room 2 per change control CC08006 • Updated attachments for ease of use.	CR08

ATTACHMENT 7 – CLEAN ROOM 1 - SURFACE SAMPLING FORM

(page 1 of 3)

Date of Sampling:
Sampler:
Media Lot#:
Exp Date:
Room State: ☐ At-Rest ☐ Operational
Start Time: | End Time:
30-35°C Incubator Serial #:
Calibration Due Date:
20-25°C Incubator Serial #:
Calibration Due Date:

Time Placed in 30-35°C:
Initials/Date:
Time Placed in 20-25°C:
Initials/Date:
Time Removed from 20-25°C:
Initials/Date:

Sample Location	Description	Results			Alert/Action	TR #
		Bacteria CFU	Mold CFU	Total CFU		
1SPF1	People Room 1 Floor 1				☐Al ☐Ac	
1SPF2	People Room 1 Floor 2				☐Al ☐Ac	
1SPF3	People Room 1 Floor 3				☐Al ☐Ac	
1SPW1	People Room 1 Wall 1				☐Al ☐Ac	
1SPW2	People Room 1 Wall 2				☐Al ☐Ac	
1SPW3	People Room 1 Wall 3				☐Al ☐Ac	
1SPD1	People Room 1 Door to Middle Room				☐Al ☐Ac	
1SMF1	Middle Room 1 Floor 1				☐Al ☐Ac	
1SMF2	Middle Room 1 Floor 2				☐Al ☐Ac	
1SMF3	Middle Room 1 Floor 3				☐Al ☐Ac	
1SMW1	Middle Room 1 Wall 1				☐Al ☐Ac	
1SMW2	Middle Room 1 Wall 2				☐Al ☐Ac	
1SMW3	Middle Room 1 Wall 3				☐Al ☐Ac	
1SMV1	Middle Room 1 Vault Front 1				☐Al ☐Ac	
1SMR1	Middle Room 1 Refrigerator Front 1				☐Al ☐Ac	
1SCH1	Clean Room 1 Hood 1				☐Al ☐Ac	
1SCH2	Clean Room 1 Hood 2				☐Al ☐Ac	
1SCH3	Clean Room 1 Hood 3				☐Al ☐Ac	

ATTACHMENT 7 – CLEAN ROOM 1 - SURFACE SAMPLING FORM

(page 2 of 3)

Sample Location	Description	Results			Alert/Action		TR #
		Bacteria CFU	Mold CFU	Total CFU			
1SCH4	Clean Room 1 Hood 4				☐Al	☐Ac	
1SCH5	Clean Room 1 Hood 5				☐Al	☐Ac	
1SCH6	Clean Room 1 Hood 6				☐Al	☐Ac	
1SCH7	Clean Room 1 Hood 7				☐Al	☐Ac	
1SCH8	Clean Room 1 Hood 8				☐Al	☐Ac	
1SCH9	Clean Room 1 Hood 9				☐Al	☐Ac	
1SCH10	Clean Room 1 Hood 10				☐Al	☐Ac	
1SCHA	Clean Room 1 Hood A				☐Al	☐Ac	
1SCHB	Clean Room 1 Hood B				☐Al	☐Ac	
1SCHC	Clean Room 1 Hood C				☐Al	☐Ac	
1SCHD	Clean Room 1 Hood D				☐Al	☐Ac	
1SCHE	Clean Room 1 Hood E				☐Al	☐Ac	
1SCHF	Clean Room 1 Hood F				☐Al	☐Ac	
1SCF1	Clean Room 1 Floor 1				☐Al	☐Ac	
1SCF2	Clean Room 1 Floor 2				☐Al	☐Ac	
1SCF3	Clean Room 1 Floor 3				☐Al	☐Ac	
1SCF4	Clean Room 1 Floor 4				☐Al	☐Ac	
1SCF5	Clean Room 1 Floor 5				☐Al	☐Ac	
1SCF6	Clean Room 1 Floor 6				☐Al	☐Ac	
1SCF7	Clean Room 1 Floor 7				☐Al	☐Ac	
1SCF8	Clean Room 1 Floor 8				☐Al	☐Ac	
1SCP1	Interior of Clean Room 1 Pass-Thru 1				☐Al	☐Ac	
1SCP2	Interior of Clean Room 1 Pass-Thru 2				☐Al	☐Ac	
1SCP3	Interior of Clean Room 1 Pass-Thru 3				☐Al	☐Ac	
1SCP4	Interior of Clean Room 1 Pass-Thru 4				☐Al	☐Ac	
1SCP5	Interior of Clean Room 1 Pass-Thru 5				☐Al	☐Ac	
1SCW1	Clean Room 1 Wall 1				☐Al	☐Ac	
1SCW2	Clean Room 1 Wall 2				☐Al	☐Ac	

ATTACHMENT 7 – CLEAN ROOM 1 - SURFACE SAMPLING FORM

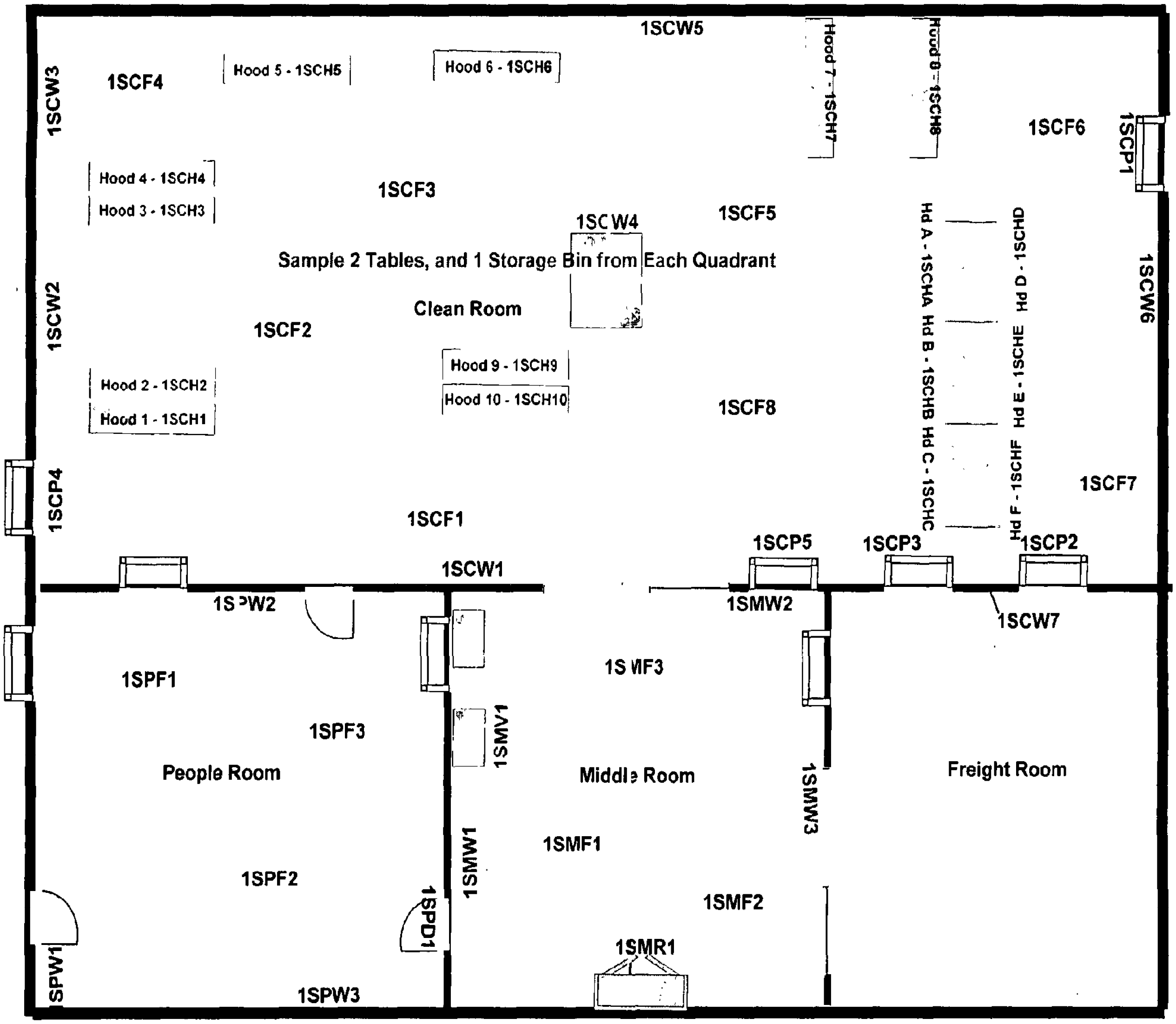
(page 3 of 3)

Sample Location	Description	Results Bacteria CFU	Mold CFU	Total CFU	Alert/Action	TR #
1SCW3	Clean Room 1 Wall 3				☐Al ☐Ac	
1SCW4	Clean Room 1 Wall 4				☐Al ☐Ac	
1SCW5	Clean Room 1 Wall 5				☐Al ☐Ac	
1SCW6	Clean Room 1 Wall 5				☐Al ☐Ac	
1SCT1	Clean Room 1Table				☐Al ☐Ac	
1SCT2	Clean Room 1 Table				☐Al ☐Ac	
1SCT3	Clean Room 1 Table				☐Al ☐Ac	
1SCT4	Clean Room 1 Table				☐Al ☐Ac	
1SCT5	Clean Room 1 Table				☐Al ☐Ac	
1SCT6	Clean Room 1 Table				☐Al ☐Ac	
1SCT7	Clean Room 1 Table				☐Al ☐Ac	
1SCT8	Clean Room 1 Table				☐Al ☐Ac	
1SCB1	Clean Room 1 Storage Bin on Table				☐Al ☐Ac	
1SCB2	Clean Room 1 Storage Bin on Table				☐Al ☐Ac	
1SCB3	Clean Room 1 Storage Bin on Table				☐Al ☐Ac	
1SCB4	Clean Room 1 Storage Bin on Table				☐Al ☐Ac	

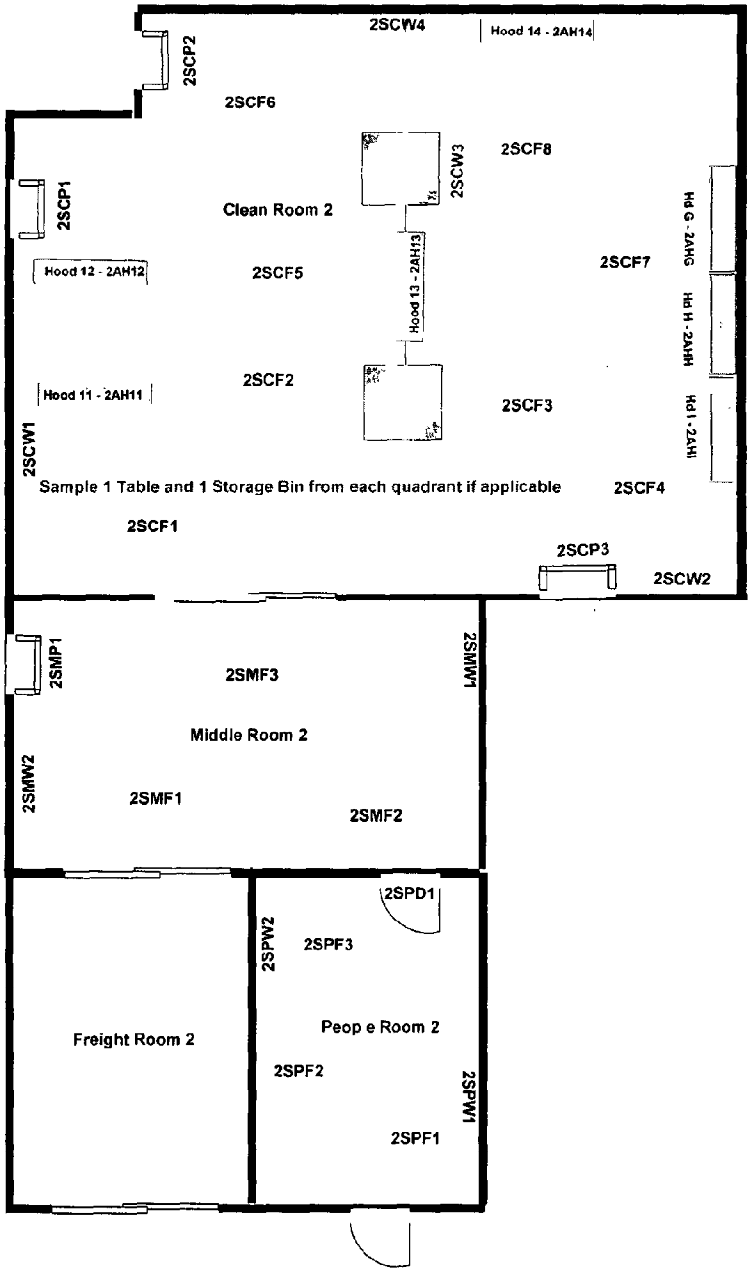
Performed By: **Date:**

Reviewed By: **Date:**

ATTACHMENT 8 – CLEAN ROOM 1 SURFACE SAMPLING MAP



ATTACHMENT 10 – CLEAN ROOM 2 - SURFACE SAMPLING MAP



Sample 1 Table and 1 Storage Bin from each quadrant if applicable

ATTACHMENT 9 – CLEAN ROOM 2 - SURFACE SAMPLING FORM

(page 1 of 2)

Date of Sampling:
Sampler:
Media Lot#:
Exp Date:
Room State: ☐ At-Rest ☐ Operational
Start Time: | End Time:
30-35°C Incubator Serial #:
Calibration Due Date:
20-25°C Incubator Serial #:
Calibration Due Date:

Time Placed in 30-35°C:
Initials/Date:
Time Placed in 20-25°C:
Initials/Date:
Time Removed from 20-25°C:
Initials/Date:

Sample Location	Description	Results			Alert/Action	TR #
		Bacteria CFU	Mold CFU	Total CFU		
2SPF1	People Room 2 Floor 1				☐Al ☐Ac	
2SPF2	People Room 2 Floor 2				☐Al ☐Ac	
2SPF3	People Room 2 Floor 3				☐Al ☐Ac	
2SPW1	People Room 2 Wall 1				☐Al ☐Ac	
2SPW2	People Room 2 Wall 2				☐Al ☐Ac	
2SPD1	People Room 2 Door to Middle Room				☐Al ☐Ac	
2SMF1	Middle Room 2 Floor 1				☐Al ☐Ac	
2SMF2	Middle Room 2 Floor 2				☐Al ☐Ac	
2SMF3	Middle Room 2 Floor 3				☐Al ☐Ac	
2SMW1	Middle Room 2 Wall 1				☐Al ☐Ac	
2SMW2	Middle Room 2 Wall 2				☐Al ☐Ac	
2SMP1	Middle Room 2 Pass-Thru 1				☐Al ☐Ac	
2SCH11	Clean Room 2 Hood 11				☐Al ☐Ac	
2SCH12	Clean Room 2 Hood 12				☐Al ☐Ac	
2SCH13	Clean Room 2 Hood 13				☐Al ☐Ac	
2SCH14	Clean Room 2 Hood 14				☐Al ☐Ac	

ATTACHMENT 8 – CLEAN ROOM 2 - SURFACE SAMPLING FORM

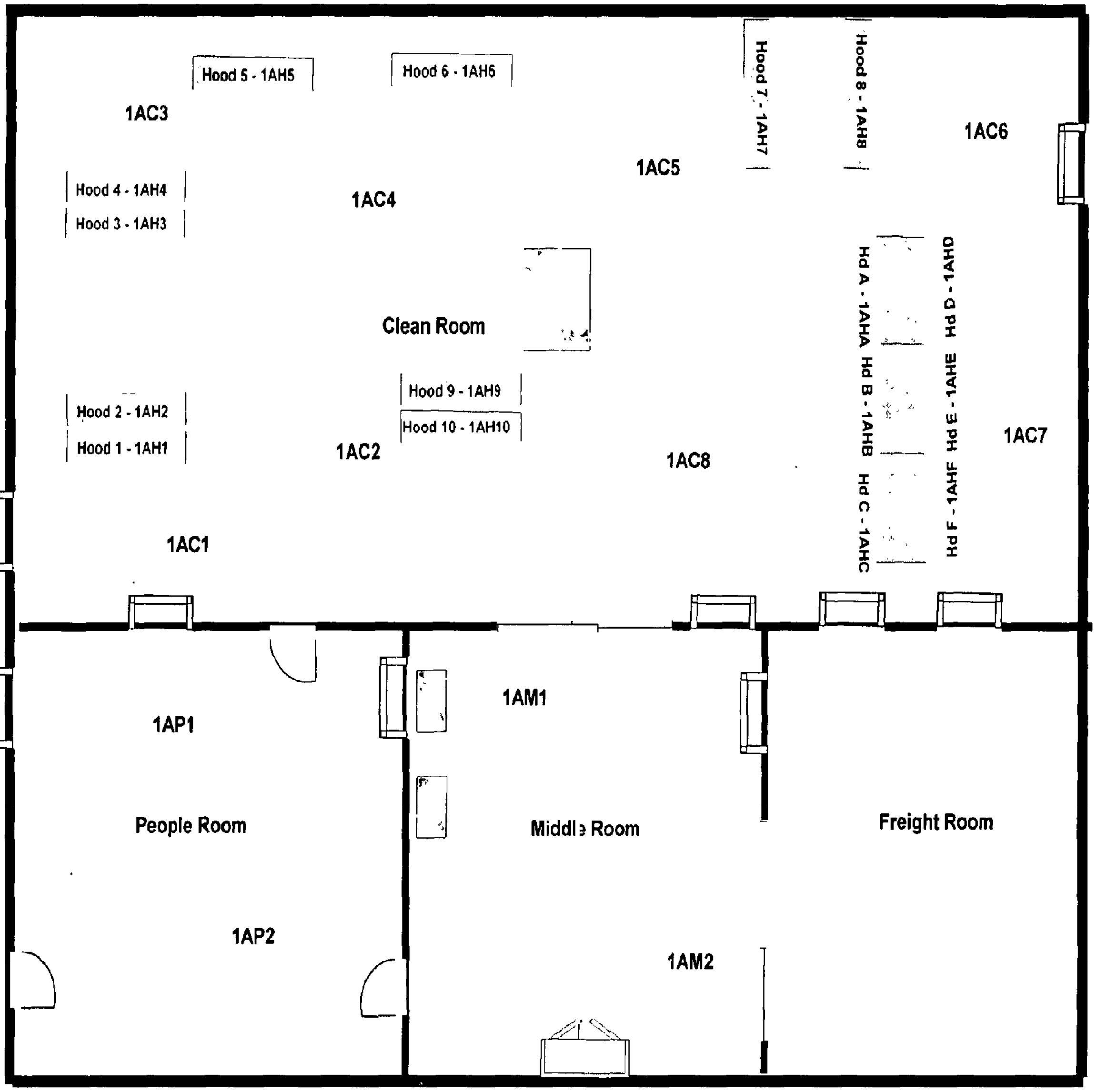
(page 2 of 2)

Sample Location	Description	Results Bacteria CFU	Mold CFU	Total CFU	Alert/Action	TR #
2SCHG	Clean Room 2 Hood G				☐Al ☐Ac	
2SCHH	Clean Room 2 Hood H				☐Al ☐Ac	
2SCHI	Clean Room 2 Hood I				☐Al ☐Ac	
2SCF1	Clean Room 2 Floor 1				☐Al ☐Ac	
2SCF2	Clean Room 2 Floor 2				☐Al ☐Ac	
2SCF3	Clean Room 2 Floor 3				☐Al ☐Ac	
2SCF4	Clean Room 2 Floor 4				☐Al ☐Ac	
2SCF5	Clean Room 2 Floor 5				☐Al ☐Ac	
2SCF6	Clean Room 2 Floor 6				☐Al ☐Ac	
2SCF7	Clean Room 2 Floor 7				☐Al ☐Ac	
2SCF8	Clean Room 2 Floor 8				☐Al ☐Ac	
2SCP1	Interior of Clean Room 2 Pass-Thru 1				☐Al ☐Ac	
2SCP2	Interior of Clean Room 2 Pass-Thru 2				☐Al ☐Ac	
2SCP3	Interior of Clean Room 2 Pass-Thru 3				☐Al ☐Ac	
2SCW1	Clean Room 2 Wall 1				☐Al ☐Ac	
2SCW2	Clean Room 2 Wall 2				☐Al ☐Ac	
2SCW3	Clean Room 2 Wall 3				☐Al ☐Ac	
2SCW4	Clean Room 2 Wall 4				☐Al ☐Ac	
2SCT1	Clean Room 2 Table______				☐Al ☐Ac	
2SCT2	Clean Room 2 Table______				☐Al ☐Ac	
2SCT3	Clean Room 2 Table______				☐Al ☐Ac	
2SCT4	Clean Room 2 Table______				☐Al ☐Ac	
2SCB1	Clean Rm 2 Storage Bin on Table ______				☐Al ☐Ac	
2SCB2	Clean Rm 2 Storage Bin on Table ______				☐Al ☐Ac	
2SCB3	Clean Rm 2 Storage Bin on Table ______				☐Al ☐Ac	
2SCB4	Clean Rm 2 Storage Bin onTable ______				☐Al ☐Ac	

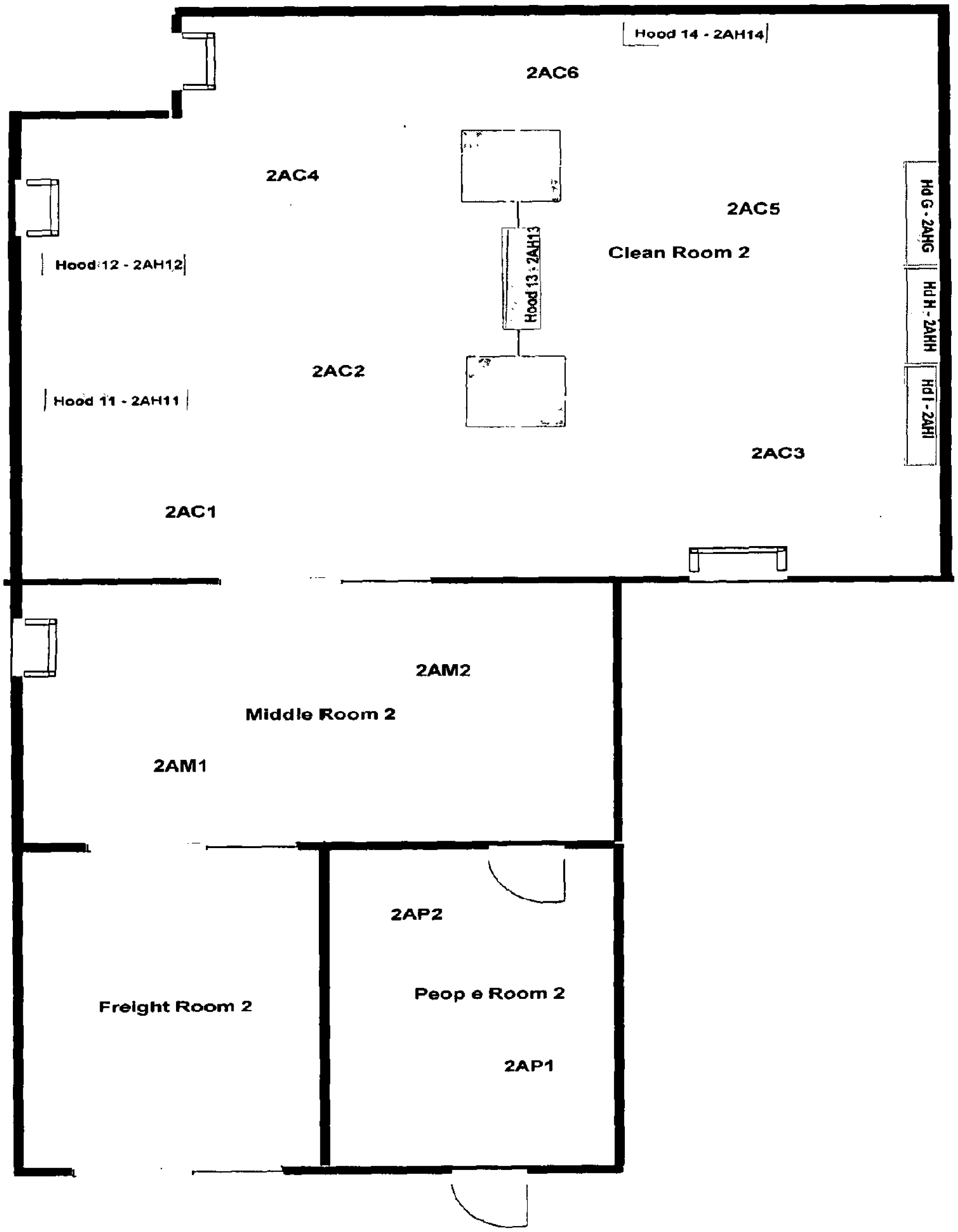
Performed By: **Date:**

Reviewed By: **Date:**

ATTACHMENT 4 – CLEAN ROOM 1 - VIABLE AIR SAMPLING MAP



ATTACHMENT 6 – CLEAN ROOM 2 - VIABLE AIR SAMPLING MAP



ATTACHMENT 5 – CLEAN ROOM 2 – VIABLE AIR SAMPLING FORM

Date of Sampling:

Sampler:

Sampler Serial #:

Calibration Due Date:

Media Lot#:

Exp Date:

Room State: ☐ At-Rest ☐ Operational

Start Time: | End Time:

30-35°C Incubator Serial #:

Calibration Due Date:

20-25°C Incubator Serial #:

Calibration Due Date:

Time Placed in 30-35°C:

Initials/Date:

Time Placed in 20-25°C:

Initials/Date:

Time Removed from 20-25°C:

Initials/Date:

Sample Location	Description	Results				Alert/Action	TR #
		Bacteria CFU	Mold CFU	Total CFU	Total CFU/ft^3		
2AP1	People Room 2 Air 1					☐Al ☐Ac	
2AP2	People Room 2 Air 2					☐Al ☐Ac	
2AM1	Middle Room 2 Air 1					☐Al ☐Ac	
2AM2	Middle Room 2 Air 1					☐Al ☐Ac	
2AC1	Clean Room 2 Air 1					☐Al ☐Ac	
2AC2	Clean Room 2 Air 2					☐Al ☐Ac	
2AC3	Clean Room 2 Air 3					☐Al ☐Ac	
2AC4	Clean Room 2 Air 4					☐Al ☐Ac	
2AC5	Clean Room 2 Air 5					☐Al ☐Ac	
2AC6	Clean Room 2 Air 6					☐Al ☐Ac	
2AH11	Hood 11					☐Al ☐Ac	
2AH12	Hood 12					☐Al ☐Ac	
2AH13	Hood 13					☐Al ☐Ac	
2AH14	Hood 14					☐Al ☐Ac	
2AHG	Hood A					☐Al ☐Ac	
2AHH	Hood B					☐Al ☐Ac	
2AHI	Hood C					☐Al ☐Ac	

Performed By: **Date:**

Reviewed By: **Date:**

ATTACHMENT 14 – ALERT FOLLOW-UP FORM

Tracking #:	Sample Date:	Sample Location/Operator Name:
Level Exceeded:		Result:
Date of follow-up cleaning:		Date of follow-up sampling:

Results of follow-up sampling:

Review: | Date

Tracking #:	Sample Date:	Sample Location/Operator Name:
Level Exceeded:		Result:
Date of follow-up cleaning:		Date of follow-up sampling:

Results of follow-up sampling:

Review: | Date

Tracking #:	Sample Date:	Sample Location/Operator Name:
Level Exceeded:		Result:
Date of follow-up cleaning:		Date of follow-up sampling:

Results of follow-up sampling:

Review: | Date

ATTACHMENT 2 – MEDIA LOG

Media Type/Catalog #	Date Received	Manufacturer	Lot Number	Quantity Rec'd (i.e.10 boxes of 50 plates)	Exp Date	Storage Conditions (°C)	CoA Rec'd and Filed	Received By (Initials/Date)

Reviewed By:

Date:

ATTACHMENT 3 – CLEAN ROOM 1 – VIABLE AIR SAMPLING FORM

(page 1 of 2)

Date of Sampling:
Sampler:
Sampler Serial #:
Calibration Due Date:
Media Lot#:
Exp Date:
Room State: ☐ At-Rest ☐ Operational
Start Time:
End Time:
30-35°C Incubator Serial #:
Calibration Due Date:
20-25°C Incubator Serial #:
Calibration Due Date:

Time Placed in 30-35°C:
Initials/Date:
Time Placed in 20-25°C:
Initials/Date:
Time Removed from 20-25°C:
Initials/Date:

Sample Location	Description	Results				Alert/Action	TR #
		Bacteria CFU	Mold CFU	Total CFU	Total CFU/ft^3		
1AP1	People Room 1 Air 1					☐Al ☐Ac	
1AP2	People Room 1 Air 2					☐Al ☐Ac	
1AM1	Middle Room 1 Air 1					☐Al ☐Ac	
1AM2	Middle Room 1 Air 1					☐Al ☐Ac	
1AC1	Clean Room 1 Air 1					☐Al ☐Ac	
1AC2	Clean Room 1 Air 2					☐Al ☐Ac	
1AC3	Clean Room 1 Air 3					☐Al ☐Ac	
1AC4	Clean Room 1 Air 4					☐Al ☐Ac	
1AC5	Clean Room 1 Air 5					☐Al ☐Ac	
1AC6	Clean Room 1 Air 6					☐Al ☐Ac	
1AC7	Clean Room 1 Air 7					☐Al ☐Ac	
1AC8	Clean Room 1 Air 8					☐Al ☐Ac	

ATTACHMENT 3 – CLEAN ROOM 1 - VIABLE AIR SAMPLING FORM

(page 2 of 2)

Sample Location	Description	Results			Total CFU/ft^3	Alert/Action	TR #
		Bacteria CFU	Mold CFU	Total CFU			
1AH1	Hood 1					☐Al ☐Ac	
1AH2	Hood 2					☐Al ☐Ac	
1AH3	Hood 3					☐Al ☐Ac	
1AH4	Hood 4					☐Al ☐Ac	
1AH5	Hood 5					☐Al ☐Ac	
1AH6	Hood 6					☐Al ☐Ac	
1AH7	Hood 7					☐Al ☐Ac	
1AH8	Hood 8					☐Al ☐Ac	
1AH9	Hood 9					☐Al ☐Ac	
1AH10	Hood 10					☐Al ☐Ac	
1AHA	Hood A					☐Al ☐Ac	
1AHB	Hood B					☐Al ☐Ac	
1AHC	Hood C					☐Al ☐Ac	
1AHD	Hood D					☐Al ☐Ac	
1AHE	Hood E					☐Al ☐Ac	
1AHF	Hood F					☐Al ☐Ac	

Performed By: **Date:**

Reviewed By: **Date:**

ATTACHMENT 12 – NON-ROUTINE SAMPLE FORM

Date of Sampling: Sampler:

Sampler Serial #: Calibration Due Date:

Media Lot#: Exp Date:

30-35°C Incubator Serial #: Calibration Due Date:

20-25°C Incubator Serial #: Calibration Due Date:

Time Placed in 30-35°C: Initials/Date:

Time Placed in 20-25°C: Initials/Date:

Time Removed from 20-25°C: Initials/Date:

Reason for Sampling:

Sample Description	Results (CFU/plate)		
	Bacteria	Mold	Total

Sample Description	Results			
	Bacteria CFU	Mold CFU	Total CFU	Total CFU/ft^3

Performed By: **Date:**

Reviewed By: **Date:**

ATTACHMENT 11 – PERSONNEL SAMPLING FORM

Date of Sampling:
Sampler:
Media Lot#:
Exp Date:
Room State: ☐ At-Rest ☐ Operational
Start Time: | End Time:
30-35°C Incubator Serial #:
Calibration Due Date:
20-25°C Incubator Serial #:
Calibration Due Date:

Time Placed in 30-35°C:
Initials/Date:
Time Placed in 20-25°C:
Initials/Date:
Time Removed from 20-25°C:
Initials/Date:

Compounder Name	Hood	Results (CFU/plate)			Alert/Action	TR#
		Bacteria	Mold	Total		
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	
					☐Al ☐Ac	

Performed By: **Date:**

Reviewed By: **Date:**

ATTACHMENT 1 – ALERT/ACTION LEVELS

Classification	Non-Viable		Viable Air (CFU/ft^3)		Surface (CFU/plate)		Personnel (CFU/plate)	
	Alert	Action	Alert	Action	Alert	Action	Alert	Action
ISO 5 (Class 100) Hoods	≥50	≥100	≥ 0.05	≥ 0.1	≥2	≥ 3	≥ 2	≥ 3
				Presence of mold		Presence of mold		Presence of mold
ISO 7 (Class 10,000) Clean Room	≥5000	≥10,000	≥ 0.25	≥ 0.5	≥ 3 - surfaces except floors	≥ 5 - surfaces except floors	N/A	N/A
			Presence of mold		≥ 5 – floors	≥10 - floors		
					Presence of mold			
ISO 8 (Class 100,000) Middle Room	≥50,000	≥100,000	≥ 1.25	≥ 2.5	≥ 5 – surfaces except floors	≥ 10 – surfaces except floors	N/A	N/A
			Presence of mold		≥ 10 – floors	≥ 20 - floors		
					Presence of mold			
ISO 9 (Class 1,000,000) People Room	≥500,000	≥1,000,000	≥ 6.25	≥ 12.5	≥ 10 – surfaces except floors	≥ 20 – surfaces except floors	N/A	N/A
					≥ 20 – floors	≥ 40 - floors		

ATTACHMENT 13 – ALERT/ACTION LOG

Tracking #	Alert or Action	Sample Date	Sample Location /Operator Name	Level Exceeded (units)	Result (units)	OOS # (If appl)	Initial/Date
	☐Alert						
	☐Action						
	☐Alert						
	☐Action						
	☐Alert						
	☐Action						
	☐Alert						
	☐Action						
	☐Alert						
	☐Action						
	☐Alert						
	☐Action						
	☐Alert						
	☐Action						
	☐Alert						
	☐Action						
	☐Alert						
	☐Action						
	☐Alert						
	☐Action						

Reviewed By:

Date:

SOP NEW/CHANGE REQUEST FORM

(Page 1 of 2)

Check one: ☐ New ☒ Change **Change Request Log Number:** 08017

SOP Number/Title: 3.030 > Environmental Monitoring of the Clean Room Facility

Version of SOP being changed: 3.0 **New Version:** 4.0

Description/Text of Change: (see attached Changed Document)

None

Reason for Change Request:
New clean room
Moved to new place

Supporting Documentation: (mark one)

☒ None Required ☐ Attached → reference (specify): ____________

Requested Implementation Date: (mark one)

☐ Less than 30 Days ☐ By Date: ____________

Annual SOP Review Requirements: (mark one)

☒ Complete review was performed to satisfy the requirements of SOP review (see page 2).

☒ Review limited to changes only, SOP review will need to be performed when scheduled.

Check Training Requirements: (mark one)

☒ Read and Understand Memo ☐ Training Session Required

Training Checklist:

☒ No Checklist is Required **OR** TC#__________ has been reviewed and:

☐ No Changes are Required

☐ Checklist needs to be Written/Changes are Required → TC change # ____________

Change Originator:	Annette M. Robinson	Annette M. Robinson	08-21-08
	Printed Name	Signature	Date
Quality Control:			
	Printed Name	Signature	Date

ORIGINAL
11-12-07

SOP REVIEW FORM

(Page 2 of 2)

SOP Number/Title:

Date Effective: **Version:** **Last Reviewed:**

SOP REVIEW – PLEASE CHECK THE FOLLOWING AS THEY ARE PERFORMED:

☐ Ensure that the purpose, scope, responsibilities, definitions, and general information sections are still accurate and current.

☐ Ensure that the responsible functional area groups are consistent with current organizational structure.

☐ Check references to ensure that they still apply, that the titles have not changed, and that the references to documents within the text are correct.

☐ Verify that all materials, equipment, reagents, etc. called for in the procedure are still available and are being used.

☐ Ensure that the current practice is reflected accurately in the procedure section of the SOP.

☐ Ensure that the procedure addresses what action to take if the task has unacceptable results.

☐ Ensure that all documentation requirements and storage/archival requirements are reflected in the SOP.

☐ Ensure that all attachments continue to be accurate and reflect current practices.

CHOOSE THE STATEMENT THAT APPLIES:

I have reviewed the above mentioned procedure and:

☐ No changes need to be implemented.

☐ SOP New/Change Request Form is attached to update the procedure, Change Request Log Number CR .

☐ SOP should be deactivated, Change Request Log Number CR .

SOP Review Performed By: **Date:**

ORIGINAL
11-2-07

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY	
SOP NUMBER: 3.030	**VERSION NUMBER: 4.0**
Sterile Laboratory	First Effective Date **03-28-06**
Originator:	Previous effective Date 11-30-07
Reviewer:	Current Effective Date 09-22-08

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for viable and non-viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644-4 "Clean Rooms and Associated Controlled Environments", Part 4

4.4 SOP 3.010 "Sterile Compounding Area Requirements"

4.5 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.6 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Viable Particle - A viable particle is a particle that contains one or more living microorganisms.

5.3 Viable Air Sampler - Device used to sample microorganisms in the air.

5.4 Non-Viable Air Sampling - Total particle count. Includes viable particles but does not test for presence of microorganisms.

5.5 Surface Contact Plate - Agar plate used to sample surfaces for microorganisms by direct application. The agar contains neutralizers to inactivate residual disinfectants.

5.6 ISO Classifications

  5.6.1 ISO Class 4 is equivalent to Class 10 (glove box, antechamber).

  5.6.2 ISO Class 6 is equivalent to Class 1,000 (main clean room).

  5.6.3 ISO Class 7 is equivalent to Class 10,000 (gown/crimp room).

  4.1.1 ISO Class 8 is equivalent to Class 100,000 (prep room).

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09-22-08

5.7 Alert Level -Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching alert level does not require investigation. (Attachment 6)

5.8 Action Level - Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action. (Attachment 6)

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled upon completion of sterile compounding and **prior to cleaning**.

6.2 Surface sampling in the glove boxes and antechambers Class 10(ISO Class 4), Class 1000 main clean room(ISO Class 6), Class10,000(ISO Class 7) gown/crimp room, Class100,000(ISO Class 8)prep room, area shall be performed weekly, **prior to cleaning**.

6.3 Sterility of 70% isopropyl alcohol (IPA) will be confirmed weekly.

6.4 Viable air sampling shall be performed weekly.

6.5 Non-Viable air sampling shall be performed at least every six months.

6.6 The Pharmacist-in-charge or the Quality Control officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 Viable air sampler with sterilized impeller and shroud (Model # SAS180)

7.4 Appropriate user manuals

7.5 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from "clean" areas to "dirty" areas.

9.0 PROCEDURE

9.1 Upon receipt of commercially prepared TSA contact plates, retain the manufacturer's Certificate of Analysis (CofA). Document receipt of the media on Receipt of Contact plates (Attachment 1).

9.2 Verify that the (CofA) documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

9.2.1 Remove two plates from new lot of media received for positive and negative controls.

9.2.2 Label one plate "Positive" and the other plate "Negative," and write the date on each plate.

9.2.3 Do not expose the agar surface of the "Negative" plate. Seal the contact plate with parafilm.

9.2.4 For the "Positive" control expose the agar to air for 15 minutes. Seal the contact plate with parafilm.

9.2.5 Incubate for 5 days at 30°C-35°C. Document on Attachment 1.

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04-22-08

9.2.6 If the positive control has no growth or the negative control has growth, the lot must be rejected.

9.2.7 Place the completed Attachment 1, along with the (CofA) in a designated binder.

9.2.8 Store all acceptable media according to the manufacturer's recommendation in a monitored refrigerator. (2°C - 8°C).

9.3 Viable Air Sampling

9.3.1 Set up the air sampler according to the manufacturer's instructions.

9.3.2 Sanitize the exterior of the air sampler prior to use with a low-lint wipe, saturated with sterile 70% IPA.

9.3.3 If the sampler is being moved from a dirty to clean location during sampling, repeat exterior sanitization.

9.3.4 Make sure the air sampler is programmed with the following parameters:

Sample Time	**Air Volume/Minute**	**Total Air Volume**
5.5 Minutes	180 Liters	1000 liters (35ft^3)

9.3.5 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.3.6 Document all data on the appropriate Attachments.

9.3.7 Obtain the appropriate quantity of media from storage.

9.3.7.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.3.7.2 Verify media is within expiration date and record media lot number and expiration date on Attachment 4.

9.3.7.3 Aseptically remove an agar contact plate from its package. Make sure that the contact plate covers remains on.

9.3.7.4 Aseptically remove the outer protective cap from the sampler and unscrew the aspirating head.

9.3.7.5 Secure the plate between the metal prongs. Once secure, remove the contact plate cover and immediately replace the aspirating head and screw on tightly.

NOTE: *Do not touch the agar surface (If agar is touched, discard the contact plate).*

9.3.8 Place the air sampler in the desired location at cart or bench top height. Orient the air sampler in a vertical position facing the ceiling and turn on.
Do not place arms over sampler while in operation.

9.3.8.1 The air sampler will automatically turn off at the conclusion of the sampling period.

9.3.8.2 Aseptically remove the contact plate from the sampler. Replace the lid of the contact plate.

9.3.8.2.1 Inspect the contact plate to ensure the impingement marks are present.

9.3.8.2.2 If impingement marks are not present, the sample is invalid and shall be repeated with a new contact plate.

9.3.8.3 Seal the contact plate with parafilm.

ORIGINAL
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9.3.8.4 Record the site location on the base of the base of the plate, initial and date. Do not record any information on the cover plate.

9.3.8.5 Invert the samples and incubate for as follows.

9.3.8.6 5 days at 30-35 °C.

NOTE: If 5th day of incubation falls on a non-business day, then the plates shall be incubated at that temperature for the remainder of the 7 days. Do not exceed 7 days of incubation.

NOTE: Samples may be shipped to a contract lab for incubation and analysis.

9.4 Non-Viable Air Sampling

9.4.1 Non-viable air sampling shall be performed every 6 months along with Room/Hood Certification.

9.4.2 Sampling shall be performed by an approved vendor using calibrated equipment.

9.4.3 File all completed documents in the designated binder.

9.5 Surface Sampling

9.5.1 Document all data on the appropriate Attachments.

9.5.2 Surface sampling in the glove boxes and antechambers - Class 10 (ISO 4), Class 1000 (ISO 6)main clean room, Class 10,000 (ISO 7)gown/crimp room, Class 100,000 (ISO 8) prep room area shall be performed weekly, **prior to cleaning**

9.5.3 Obtain the appropriate quantity of contact plates from storage.

9.5.3.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.5.3.2 Verify media is within expiration date and record media lot number and expiration date on appropriate Attachment.

9.5.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.5.5 Sampling technique:

9.5.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface for 10 seconds.

9.5.5.2 Replace the cover and seal the plate with parafilm.

9.5.5.3 Record the site location on the base of the plate. Do not record any information on the cover of the plate.

9.5.5.4 Clean the sample site with sterile 70% IPA before proceeding to the next site.

9.5.6 Incubate for 5 days 30°C-35°C.

9.5.7 Record surface sampling results on Attachment 2, and file all completed documents in the EM binder.

9.6 Confirm the Sterility of 70% IPA

9.6.1 Refer to the appropriate Attachment for Surface Sampling Log

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AMW 04-22-08

9.6.2 Obtain two contact plates from storage and test two random sterile 70% IPA bottles.

9.6.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.6.2.2 Verify media is within expiration date, and record media lot number and expiration date on Attachment 2.

9.6.3 Aseptically remove the contact plate cover.

NOTE: *Do not touch the agar surface (If agar is touched, discard the contact plate).*

9.6.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.6.5 Replace the cover and seal the plate with parafilm.

9.6.6 Label the base of the plate with "IPA" and the IPA lot number/expiration date. Do not record any information on the cover of the plate.

9.6.7 Incubate for 5 days at 30°C-35°C.

9.6.8 Record results on Attachment 2, and file all completed documents in the EM binder.

9.7 Personnel Monitoring

9.7.1 Refer to the Clean Room Facility Personnel Touch Plate Log (Attachment 5).

9.7.2 Obtain the appropriate quantity of contact plates from storage.

9.7.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.7.2.2 Verify media is within expiration date.

9.7.2.3 Label the base of the contact plate with the date, the pharmacist/technician initials, the hand sampled and what product is being compounded.

9.7.2.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.7.3 Replace the cover and seal the plate with parafilm.

9.7.4 Incubate for 5 days at 30°C-35°C.

9.7.5 Record personnel monitoring results on Attachment 5 and file all completed documents in the EM binder.

9.8 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

9.9 Alert and Action Limits

9.9.1 Air Sampling (Viable)

9.9.2 Calculate the level of viable airborne particulates as CFU per cubic foot. The volume of air sampled in the Class 10 (ISO 4) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

9.9.2.1 The alert/action limits for air sampling should be derived from historical data. * **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 6).**

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9.9.3 Surface and Personnel Monitoring

9.9.3.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.9.3.2 The alert/action limits for surface and personnel monitoring should be derived from historical data. * **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 6).**

9.10 Investigation and Corrective Actions

9.10.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

9.10.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized.

9.10.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.3.1 Review of sanitation procedures

9.10.3.2 Review of sampling technique

9.10.3.3 Review of clean room personnel

9.10.3.4 Inspection of sampling media

9.10.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.4.1 Identification of microbial isolates to determine origin

9.10.4.2 Review of pressure differential information

9.10.4.3 Review of HEPA and clean room certification

9.10.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.10.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

9.11 Non-Routine Samples

9.11.1 Non-routine samples that are not listed on the Viable and Surface Sampling Forms may be taken at a desired location.

9.11.2 Take the sample according to the appropriate air or surface sampling procedure above.

9.11.3 Document the sample location, sampling (air/surface), and results on Attachment 3.

9.11.4 Non-routine samples are investigational and shall not be compared to alert/action values. Do not generate an alert or action as described in 9.10 for non-routine samples.

9.12 Reporting Results

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04-22-08

9.12.1 Remove samples from the incubator. Record stop times on the appropriate attachment.

9.12.2 Count all colonies on the plate and document results for each category below.

- Bacteria
- Mold (Count or indicate presence)
- Total Counts of Bacteria and Mold combined

10.0 ATTACHMENTS

10.1 Attachment 1 - Receipt of Contact Plates
10.2 Attachment 2 - Clean Room Surface Sampling Diagram and Form
10.3 Attachment 3 - Non-Routine Air/Surface Sample Form
10.4 Attachment 4 - Clean Room Viable Air Sampling Diagram and Form
10.5 Attachment 5 - Clean Room Facility Personnel Touch Plate Log
10.6 Attachment 6 - Levels for Air and Surface Monitoring

1.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06012
2.0	04/06/06	Updated section 9.3 and attachment 1 to include positive/negative controls. Updated sample identification labels and schematic maps on attachments 2, 3, 4 and 5.	CR06053
3.0	11/30/07	Taking out TSA Strips, non-viable samples, fixing iso/ classes not correct	CR07018
4.0	09-22-07	Re did attachments for new clean room, Minor changes	CR08017

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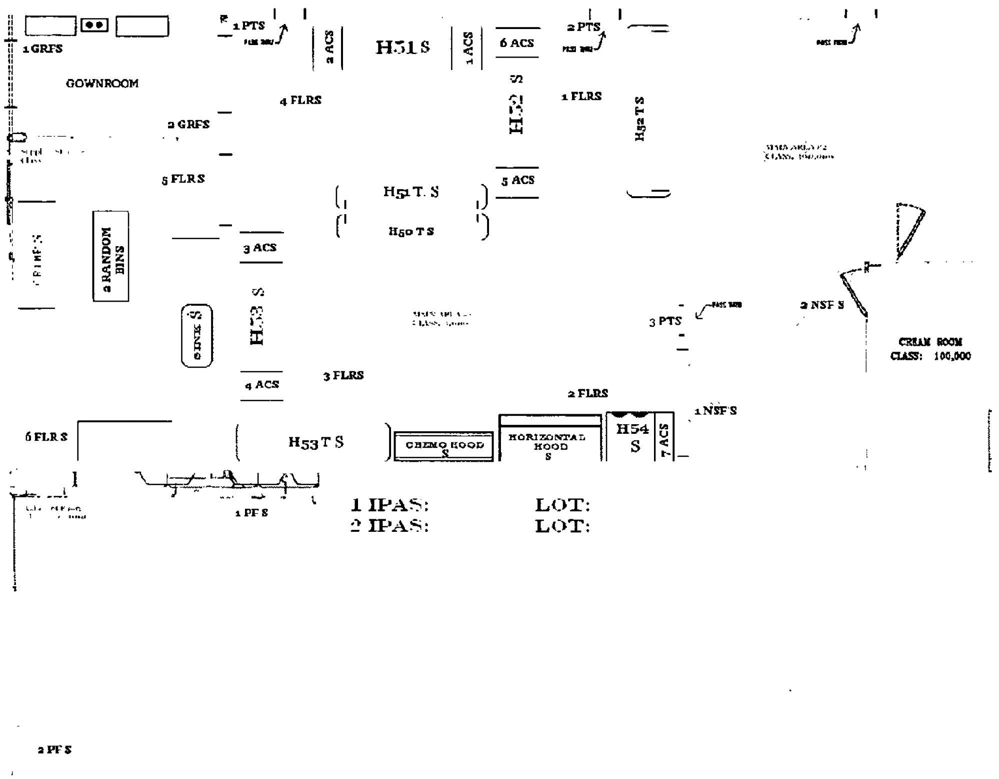
RECEIPT OF CONTACT PLATES - ATTACHMENT 1

Quantity Rec'd (i.e. boxes of 50 plates)	*Manufacturer*	*Lot Number*	*Expiration Date*	*Received By (Initials/Date)*	*Incubation Dates of Positive and Negative Controls 30°C-35°C*	*Positive Control*	*Negative Control*	*Results (CFU)*
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject

Quality Control: **Date:**
Revi wed By: **Date:**

ORIGINAL
MMK 04-22-08

Clean Room Surface Sampling Diagram



1 IPAS: LOT:
2 IPAS: LOT:

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RWK 04-22-06

CLEAN ROOM SURFACE SAMPLING - ATTACHMENT 2

(Page 1 of 2)

Sample Location	Description	Results			Alert/ Action
		Bacteria CFU	Mold CFU	Total CFU	
H51S	Hood 1				☐Al ☐Ac
H52S	Hood 2				☐Al ☐Ac
H53S	Hood 3				☐Al ☐Ac
H54S	Hood 4				☐Al ☐Ac
1ACS	Hood 1 Antechamber (Right Side)				☐Al ☐Ac
2ACS	Hood 1 Antechamber (Left Side)				☐Al ☐Ac
3ACS	Hood 2 Antechamber (Right Side)				☐Al ☐Ac
4ACS	Hood 2 Antechamber (Left Side)				☐Al ☐Ac
5ACS	Hood 3 Antechamber (Left Side)				☐Al ☐Ac
6ACS	Hood 3 Antechamber (Right Side)				☐Al ☐Ac
7ACS	Hood 4 Antechamber				☐Al ☐Ac
ChemoS	Chemo Hood				☐Al ☐Ac
HorizS	Horizontal Hood				☐Al ☐Ac
H50TS	Table 1				☐Al ☐Ac
H51TS	Table 2				☐Al ☐Ac
H52TS	Table 3				☐Al ☐Ac
H53TS	Table 4				☐Al ☐Ac
1PTS	Pass - thru				☐Al ☐Ac
2PTS	Pass - thru				☐Al ☐Ac
3PTS	Pass - thru				☐Al ☐Ac

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04-22-08

CLEAN ROOM SURFACE SAMPLING - ATTACHMENT 2

(Page 2 of 2)

Sample Location	Description	Results Bacteria CFU	Results Mold CFU	Results Total CFU	Alert/ Action
SinkS	Sink in Crimp Room				☐Al ☐Ac
CrimpS	Crimping Bench				☐Al ☐Ac
1RBS	Random Bin				☐Al ☐Ac
2RBS	Random Bin				☐Al ☐Ac
1GRFS	Gown Room – Near Hall				☐Al ☐Ac
2GRFS	Gown Room – Near Clean room				☐Al ☐Ac
1PFS	Prep Room – Near Incubator				☐Al ☐Ac
2PFS	Prep Room – Near Warehouse				☐Al ☐Ac
1FLRS	Clean Room Floor				☐Al ☐Ac
2FLRS	Clean Room Floor				☐Al ☐Ac
3FLRS	Clean Room Floor				☐Al ☐Ac
4FLRS	Clean Room Floor				☐Al ☐Ac
5FLRS	Clean Room Floor				☐Al ☐Ac
6FLRS	Clean Room Floor				☐Al ☐Ac
1IPAS	Isopropyl Alcohol				☐Al ☐Ac
2IPAS	Isopropyl Alcohol				☐Al ☐Ac

Alert		Action
1 CFU	ISO 4 (class 10) Glove box, Antechambers	2+ CFU
3 CFU	ISO 6 (class 1,000) Main Clean room	5+ CFU
5 CFU	ISO 7 (class 10,000) Gown room, Crimp room	7+ CFU
8 CFU	ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling: Media Lot: Exp Date:

Quality Control: Date:
Reviewed By: Date:

ORIGINAL
AWB 04-22-06

NON-ROUTINE AIR/SURFACE SAMPLE FORM - ATTACHMENT 3

Surface Sample Location	Description	Results Bacteria CFU	 Mold CFU	 Total CFU

Date of Sampling: Media Lot#: Exp Date:
Date placed in incubator: (Incubate for 5 days at 30-35 °C)
Reason for Sampling:

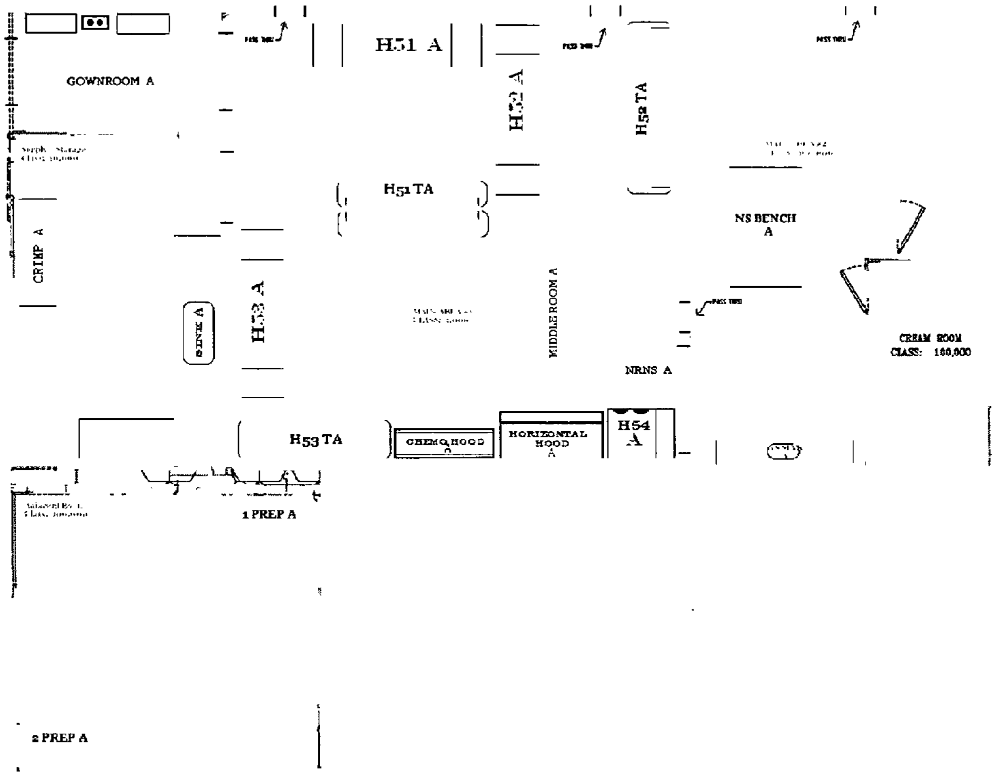
Air Sample Location	Description	Results Bacteria CFU	 Mold CFU	 Total CFU

Date of Sampling: Media Lot#: Exp Date:
Sampler Mfg/Model: Calibration Due Date:
Date placed in incubator: (Incubate for 5 days at 30-35 °C)
Reason for Sampling:

Quality Control: Date:
R viewed By: Date:

04-22-08

Clean Room Viable Air Sampling Diagram



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04-22-08

CLEAN ROOM VIABLE AIR SAMPLING - ATTACHMENT 4

Page 1 of 1

Sample Location	Description	Results			Alert/Action
		Bacteria CFU	Mold CFU	Total CFU	
H51A	Hood 1				☐Al ☐Ac
H52A	Hood 2				☐Al ☐Ac
H53A	Hood 3				☐Al ☐Ac
H54A	Hood 4				☐Al ☐Ac
ChemoA	Chemo Hood				☐Al ☐Ac
HorizA	Horizontal Hood				☐Al ☐Ac
H51TA	Table 2				☐Al ☐Ac
H52TA	Table 3				☐Al ☐Ac
H53TA	Table 4				☐Al ☐Ac
GownroomA	Gowning Area				☐Al ☐Ac
SinkA	Sink Area				☐Al ☐Ac
CrimpA	Crimping Bench				☐Al ☐Ac
MiddleroomA	Middle of Room				☐Al ☐Ac
NRNSA	Near Non-Sterile Lab				☐Al ☐Ac
1PrepA	Prep Room – Near Incubator				☐Al ☐Ac
2PrepA	Prep Room – Near Warehouse				☐Al ☐Ac

Alert	**Action**
-1 CFU ISO 4 (class 10) Glove box, Antechambers	- 2+ CFU
2 CFU ISO 6 (class 1,000) Main Clean room	3+ CFU
5 CFU ISO 7 (class 10,000) Gown room, Crimp room	8+ CFU
8 CFU ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling: Media Lot: Exp Date:
Sampler Mfg/Model: Serial #: Calibration Due Date:

Quality Control: Date:
Reviewed By: Date:

ORIGINAL
AMK
04-22-08

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATE LOG - ATTACHMENT 5

Media Lot # and Exp Date	Rph/Tech	Location and Product Being worked on	Incubation for 5 days at 30°C - 35°C	Results (CFU)	Alert / Action
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac

Alert Level 1+ CFU
Action Level 2+ CFU

ORIGINAL
04-22-08

Quality Control: Date:

Reviewed By: Date:

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY
SOP NUMBER: 3.030 **VERSION NUMBER: 4.0**

LEVELS FOR AIR AND SURFACE MONITORING - ATTACHMENT 6

Note: ** Alert/Action Levels are to be determined after historical data is collected**

Levels for Air Sampling

Classifications	Alert Level	Action Level
ISO 4 (Class 10) Glove box, Antechambers	1 CFU	2+ CFU
ISO 6 (Class 1,000) Main Clean Room	2 CFU	3+ CFU
ISO 7(Class 10,000) Gown room, Crimp Room	5 CFU	8+ CFU
ISO Class 8 (Class 100,000) Prep Room	8 CFU	10+ CFU

Levels for Surface Sampling

Classifications			Alert Level	Action Level
ISO 4 (Class 10) Glove box, Antechambers			1 CFU	2+ CFU
ISO 6 (Class 1,000) Main Clean Room			3 CFU	5+ CFU
ISO 7(Class 10,000) Gown room, Crimp Room			5 CFU	7+ CFU
ISO Class 8 (Class 100,000) Prep Room			8 CFU	10+CFU

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04-22-06

SOP CHANGE REQUEST

(Page 1 of 2)

Check one: ☐ New ☒ Change **Change Request Log Number:** 07018

SOP Number/Title: 3.030
Environmental Monitoring of the Clean Room Facility

Version of SOP being changed: 2.0 **New Version:** 3.0

Description/Text of Change: (see attached Changed Document)
Taking out TSA strips and Non-viable Sample
Fixing ISO classes / They were incorrect

Reason for Change Request:
Don't need, changes and revisions
Fixing ISO classes / were in Error some

Supporting Documentation: (mark one)

☒ None Required ☐ Attached → reference (specify):

Requested Implementation Date: (mark one)

☒ Less than 30 Days ☐ By Date:

Annual SOP Review Requirements: (mark one)

☐ Complete review was performed to satisfy the requirements of SOP review (see page 2).

☒ Review limited to changes only, SOP review will need to be performed when scheduled.

Check Training Requirements: (mark one)

☒ Read and Understand Memo ☐ Training Session Required

Training Checklist:

☐ No Checklist is Required OR TC# has been reviewed and:

☐ No Changes are Required

☐ Checklist needs to be Written/Changes are Required → TC change #

Change Originator: Annette M. Robinson (Printed Name) Annete M. Robinson (Signature) 10-10-07 (Date)

Quality Control: Annette M. Robinson (Printed Name) Annette M. Robinson (Signature) 10-10-07 (Date)

ORIGINAL
AA 03-07-06

New England Compounding Center

SOP REVIEW FORM

(Page 2 of 2)

SOP Number/Title:

Date Effective: **Version:** **Last Reviewed:**

SOP REVIEW – PLEASE CHECK THE FOLLOWING AS THEY ARE PERFORMED:

- ☐ Ensure that the purpose, scope, responsibilities, definitions, and general information sections are still accurate and current.
- ☐ Ensure that the responsible functional area groups are consistent with current organizational structure.
- ☐ Check references to ensure that they still apply, that the titles have not changed, and that the references to documents within the text are correct.
- ☐ Verify that all materials, equipment, reagents, etc. called for in the procedure are still available and are being used.
- ☐ Ensure that the current practice is reflected accurately in the procedure section of the SOP.
- ☐ Ensure that the procedure addresses what action to take if the task has unacceptable results.
- ☐ Ensure that all documentation requirements and storage/archival requirements are reflected in the SOP.
- ☐ Ensure that all attachments continue to be accurate and reflect current practices.

CHOOSE THE STATEMENT THAT APPLIES:

I have reviewed the above mentioned procedure and:

- ☐ No changes need to be implemented.
- ☐ SOP Change Request is attached to update the procedure, Change Request Log Number CR
- ☐ SOP should be obsoleted, Change Request Log Number CR

SOP Review Performed By: **Date:**

ORIGINAL
AA 03-07-06

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 **VERSION NUMBER: 3.0**

Sterile Laboratory
Originator:
Reviewer:

First Effective Date **03-28-06**
Previous effective Date 04-06-06
Current Effective Date 11-30-07

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644-4 "Clean Rooms and Associated Controlled Environments, Part 4

4.4 SOP 3.010 "Sterile Compounding Area Requirements"

4.5 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.6 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Viable Air Sampler – Device used to provide quantitative analysis of viable airborne particles

5.3 Surface Contact Plate – Device of known surface area providing a convex surface to remove viable particles from a flat work surface

5.4 ISO Classifications

- 5.4.1 ISO Class 4 is equivalent to Class 10(Glove box, antechamber).
- 5.4.2 ISO Class 7 is equivalent to Class 10,000(Clean room).
- 5.4.3 ISO Class 8 is equivalent to Class 100,000(Anteroom).

ORIGINAL
11-30-07

5.5 Alert Level – Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching alert level does not require investigation. (See Attachment 7)

5.6 Action Level – Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action. (See Attachment 7)

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled once per person daily upon completion of sterile compounding and **prior to cleaning**.

6.2 Surface sampling in the glove boxes and antechambers Class10(ISO Class 4) clean room Class10,000(ISO Class 7) and anteroom Class100,000(ISO Class 8) area shall be performed weekly, **prior to cleaning**.

6.3 Sterility of 70% isopropyl alcohol (IPA) will be confirmed weekly.

6.4 Viable air sampling shall be performed weekly.

6.5 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 Viable air sampler with sterilized impeller and shroud (Model # SAS180)

7.4 Appropriate user manuals

7.5 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from "clean" areas to "dirty" areas.

9.0 PROCEDURE

9.1 Upon receipt of commercially prepared TSA contact plates, retain the manufacturer's certificate of analysis. Document receipt of the media on Receipt of Contact plates (Attachment 1).

9.2 Verify that the certificate of analysis documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

- 9.2.1 Remove two plates from new lot of media received for positive and negative controls.
- 9.2.2 Label one plate "Positive" and the other plate "Negative," and write the date on each plate.
- 9.2.3 Do not expose the agar surface of the "Negative" plate. Seal the contact plate with parafilm.
- 9.2.4 For the "Positive" control expose the agar to air for 15 minutes. Seal the contact plate with parafilm.
- 9.2.5 Incubate the positive/negative control for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. document on Attachment 1.

ORIGINAL
11-30-07

9.2.6 If the positive control has no growth or the negative control has growth, the lot must be rejected.

9.2.7 Place the completed Attachment 1, along with the certificate of analysis, in a designated binder.

9.2.8 Store all acceptable media according to the manufacturer's recommendation (usually 2°C-8°C) in a monitored refrigerator.

9.3 Viable Air Sampling

9.3.1 Refer to the appropriate Clean Room Facility Air Sampling Log (Attachments 2 and 3).

9.3.2 Verify that the air sampler is within calibration and document the manufacturer/model, serial number, and calibration due date on Attachments 2 and 3.

9.3.3 Sanitize the air sampler exterior prior to entry into the clean room facility.

9.3.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.3.5 Obtain the appropriate quantity of media from storage.

9.3.5.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.3.5.2 Verify media is within expiration date and record media lot number and expiration date on Attachments 2 and 3.

9.3.5.3 Aseptically remove an agar contact plate from its package. Do not touch the agar surface (If agar is touched, discard the contact plate and begin again).

9.3.5.4 Aseptically remove the cap from the sampler and secure the plate between the metal prongs

9.3.6 Set up the air sampler according to the manufacturer's instructions. The volume of air sampled in the Class 10(ISO Class 4) area will be 284 liters(10 cubic feet) and all other locations will be 142 liters(5 cubic feet).

9.3.6.1 Place the viable air sampler in the desired location and turn on. Begin in the Class 10(ISO Class 4) glove box, followed by the Class 10,000(ISO Class 7) clean room, then the Class 100,000(ISO Class 8) anteroom. . **Do not place arms over sampler while in operation.**

9.3.6.2 The air sampler will automatically turn off at the conclusion of the sampling period.

9.3.6.3 Aseptically remove the contact plate from the sampler. Replace the lid of the contact plate.

9.3.6.4 Seal the contact plate with Para film.

9.3.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C.

9.3.8 Record viable air sampling results on Attachments 2 and 3, and file all completed documents in the EM binder.

9.4 Surface Sampling

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4-30-07

9.4.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 4 and 5).

9.4.2 Surface sampling in the glove boxes and antechambers Class 10 (ISO Class 4), clean room Class 10,000 (ISO Class 7) and anteroom Class 100,000 (ISO Class 8) area shall be performed weekly, **prior to cleaning**

9.4.3 Obtain the appropriate quantity of contact plates from storage.

9.4.3.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.4.3.2 Verify media is within expiration date and record media lot number and expiration date on Attachments 4 and 5.

9.4.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.4.5 Sampling technique:

9.4.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface for 10 seconds.

9.4.5.2 Replace the cover and seal the plate with parafilm.

9.4.5.3 Record the site location on the base of the plate. Do not record any information on the cover of the plate.

9.4.5.4 Clean the sample site with sterile 70% IPA before proceeding to the next site.

9.4.6 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C.

9.4.7 Record surface sampling results on Attachments 4 and 5, and file all completed documents in the EM binder.

9.5 Confirm the Sterility of 70% IPA

9.5.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 4 and 5).

9.5.2 Obtain two contact plates from storage and test two random sterile70% IPA bottles.

9.5.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.5.2.2 Verify media is within expiration date, and record media lot number and expiration date on Attachments 4 and 5.

9.5.3 Aseptically remove the contact plate cover. Do not touch the agar surface (If agar is touched, discard the plate and begin again).

9.5.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.5.5 Replace the cover and seal the plate with parafilm.

9.5.6 Label the base of the plate with "IPA" and the IPA lot number/expiration date. Do not record any information on the cover of the plate.

ORIGINAL
11-30-07

9.5.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C.

9.5.8 Record results on Attachments 4 and 5, and file all completed documents in the EM binder.

9.6 Personnel Monitoring

9.6.1 Refer to the Clean Room Facility Personnel Touch Plate Log (Attachment 6).

9.6.2 Obtain the appropriate quantity of contact plates from storage.

9.6.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.6.2.2 Verify media is within expiration date.

9.6.2.3 Label the base of the contact plate with the date, the pharmacist/technician initials and the hand sampled.

9.6.2.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.6.3 Replace the cover and seal the plate with parafilm.

9.6.4 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C.

9.6.5 Record personnel monitoring results on Attachment 6 and file all completed documents in the EM binder.

9.7 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

9.8 Alert and Action Limits

9.8.1 Air Sampling (Viable)

9.8.2 Calculate the level of viable airborne particulates as CFU per cubic foot. The volume of air sampled in the Class 10 (ISO Class 4) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

9.8.2.1 The alert/action limits for air sampling should be derived from historical data. *** Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 7).**

9.8.3 Surface and Personnel Monitoring

9.8.3.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.8.3.2 The alert/action limits for surface and personnel monitoring should be derived from historical data. *** Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 7).**

9.9 Investigation and Corrective Actions

9.9.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

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11-30-07

9.9.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized.

9.9.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.9.3.1 Review of sanitation procedures
9.9.3.2 Review of sampling technique
9.9.3.3 Review of clean room personnel
9.9.3.4 Inspection of sampling media

9.9.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.9.4.1 Identification of microbial isolates to determine origin
9.9.4.2 Review of pressure differential information
9.9.4.3 Review of HEPA and clean room certification
9.9.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.9.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

10.0 ATTACHMENTS

10.1 Attachment 1 – Receipt of Contact Plates
10.2 Attachment 2 – Clean Room 1 Air Sampling Log
10.3 Attachment 3 – Clean Room 2 Air Sampling Log
10.4 Attachment 4 – Clean Room 1 Surface Sampling Log
10.5 Attachment 5 – Clean Room 2 Surface Sampling Log
10.4 Attachment 6 – Clean Room Facility Personnel Touch Plate Log
10.5 Attachment 7 – USP Proposed Levels for Air and Surface Monitoring

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11-30-07

11.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06012
2.0	04/06/06	Updated section 9.3 and attachment 1 to include positive/negative controls. Updated sample identification labels and schematic maps on attachments 2, 3, 4 and 5.	CR06053
3.0	11-30-07	Taking out TSA Strips, non-viable samples, fixing iso/ classes not correct	CR07018

ORIGINAL
11-30-07

RECEIPT OF CONTACT PLATES

Manufacturer	Lot Number	Expiration Date	Received By (Initials/Date)	Incubation Dates of Positive and Negative Controls	Positive Control	Negative Control	Result
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject

Performed By: **Date:**

Reviewed By: **Date:**

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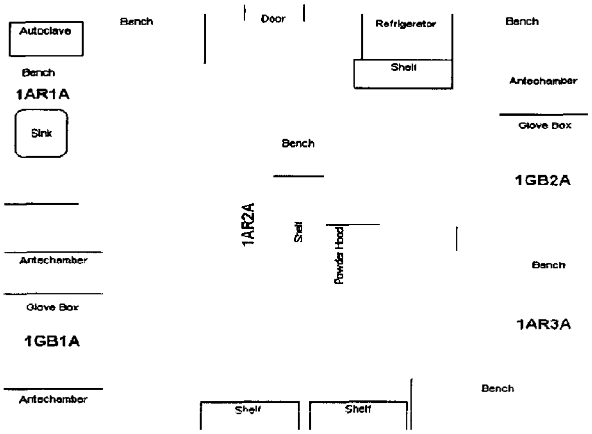
11-30-07

CLEAN ROOM 1 AIR SAMPLING LOG



VIABLE SAMPLES

Sample	Location	Incubation Dates 20°C-25°C (room temperature)	 30°C-35°C (incubate)	Results (CFU)
1GB1A	ISO Class 4 Glove Box			
1GB2A	ISO Class 4 Glove Box			
1AR1A	ISO Class 7 Clean Room			
1AR2A	ISO Class 7 Clean Room			
1AR3A	ISO Class 7Clean Room			

Alert 1 CFU (ISO Class 4 Glove Box)
1-4 CFU (ISO Class 7 Clean Room)

Action 2+ CFU (ISO Class 4 Glove Box)
5+ CFU (ISO Class 7 Clean Room)

Viable Air Sampler
Mfg./Model:
Serial #:
Calibration Due:
Media Lot #/Expiration Date:

Comments:

Performed By:
Date:

Reviewed By:
Date:

New England Compounding Center

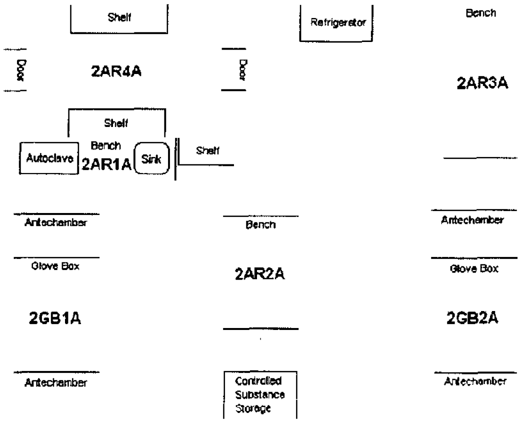
SOP 3.030

Version 3.0

ORIGINAL
11-30-07

Attachment 2

CLEAN ROOM 2 AIR SAMPLING LOG



Sample	Location	VIABLE SAMPLES Incubation Dates 20°C-25°C (room temperature)	 30°C-35°C (incubate)	Results (CFU)
2GB1A	ISO Class 4 Glove Box			
2GB2A	ISO Class 4 Glove Box			
2AR1A	ISO Class 7 Room			
2AR2A	ISO Class 7 Room			
2AR3A	ISO Class 7 Room			
2AR4A	ISO Class 8 Room			

Alert 1 CFU (ISO Class 4 Glove Box, Antechamber) **Action** 2+ CFU (ISO Class 4 Glove Box, Antechamber)
1-2 CFU (ISO Class 7 Clean Room) 3+ CFU (ISO Class 7 Clean Room)

Viable Air Sampler

Mfg./Model:

Serial #: Calibration Due:

Media Lot #/Expiration Date:

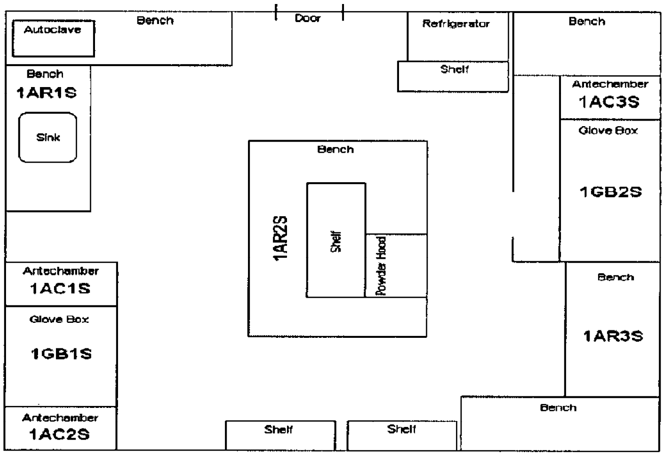
Comments:

Performed By: **Date:**

Reviewed By: **Date:**

ORIGINAL 4-30-07

CLEAN ROOM 1 SURFACE SAMPLING LOG



Sample	Location	Incubation Dates 20°C-25°C (room temperature)	30°C-35°C (incubate)	Results (CFU)
1GB1S	ISO Class 4 Glove Box			
1GB2S	ISO Class 4 Glove Box			
1AC1S	ISO Class 7 Antechamber			
1AC2S	ISO Class 7 Antechamber			
1AC3S	ISO Class 7 Antechamber			
1AR1S	ISO Class 7 Room			
1AR2S	ISO Class 7 Room			
1AR3S	ISO Class 7 Room			
1IPA1	Sterile 70% IPA			
1IPA2	Sterile 70% IPA			

Alert 1 CFU (ISO Class 4 Glove Box, Antechamber) **Action** 2+ CFU (ISO Class 4 Glove Box, Antechamber)
1-4CFU (ISO Class 7 Clean Room) 5+ CFU (ISO Class 7 Clean Room)

Media Lot #/Expiration Date: ______________________________

Comments:

____

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Performed By: ______________________________ **Date:** ______________

Reviewed By: ______________________________ **Date:** ______________

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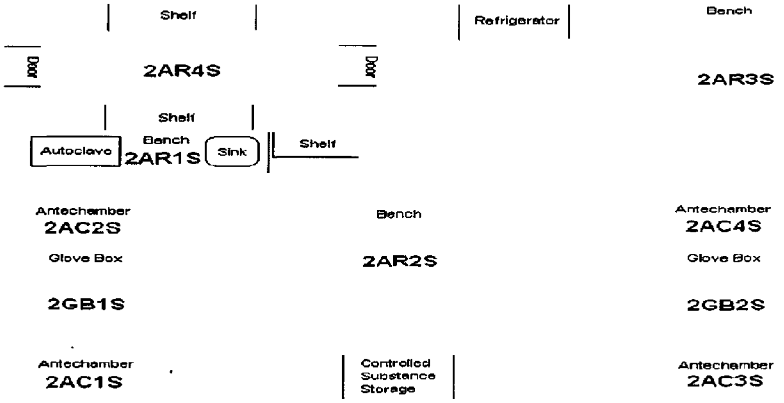
CLEAN ROOM 2 SURFACE SAMPLING LOG



Sample	Location	Incubation Dates		Results (CFU)
		20°C-25°C (room temperature)	30°C-35°C (incubate)	
2GB1S	ISO Class 4 Glove Box			
2GB2S	ISO Class 4 Glove Box			
2AC1S	ISO Class 7 Antechamber			
2AC2S	ISO Class 7 Antechamber			
2AC3S	ISO Class 7 Antechamber			
2AC4S	ISO Class 7 Antechamber			
2AR1S	ISO Class 7 Room			
2AR2S	ISO Class 7 Room			
2AR3S	ISO Class 7 Room			
2AR4S	ISO Class 8 Room (Shelf)			
2IPA1	Sterile 70% IPA			
2IPA2	Sterile 70% IPA			

Alert 1 CFU (ISO Class 4 Glove Box, Antechamber) **Action** 2+ CFU (ISO Class 4 Glove Box, Antechamber)
1-3 CFU (ISO Class 7 Clean Room) 4+ CFU (ISO Class 7 Clean Room)

Media Lot #/Expiration Date:

Comments:

Performed By: **Date:**

Reviewed By: **Date:**

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RMR 4-30-07

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATE LOG

Media Lot # and Expiration Date	Rph / Tech	Incubation Dates 20°C-25°C (room temperature)	Incubation Dates 30°C-35°C	Results (CFU)

Alert Level **1 CFU**

Action Level **2+ CFU**

Prepared By: **Date:**

Reviewed By: **Date:**

ORIGINAL 11-30-07

LEVELS FOR AIR AND SURFACE MONITORING

Note: Alert/Action Levels are to be determined after historical data is collected.

Levels for Air Sampling

Classifications	**Alert Level**	**Action Level**
Critical Areas Class 10 ISO Class 4) (glove box, antechamber)	**CR1/CR2 1 CFU**	**CR1/CR2 2+ CFU**
Non-Critical Areas Class 10,000 (ISO Class 7) (clean room)	**CR1 1-4 CFU** **CR2 1-2 CFU**	**CR1 5+ CFU** **CR2 3+ CFU**
Support Areas Class 100,000 (ISO Class 8) (anteroom)	**CR2 1-3N/A**	**CR2 4+CFU**

Levels for Surface Sampling

Classifications	**Alert Level**	**Action Level**
Critical Areas Class 10 (ISO Class 4) (glove box, antechamber)	**CR1/CR2 1CFU**	**2+ CFU**
Non-Critical Areas Class 10,000 (ISO Class 7) (clean room)	**CR1 1-4CFU CR2 1-3CFU**	**5+ CFU** **4+ CFU**
Support Areas Class 100,000 (ISO Class 8)) (anteroom)	**CR2 1-3CFU**	**4+CFU**

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11-30-07

Ⓘ Alert -(A) (Surface)   Action -(A) (Surface)

(1.) Class-10 chamber	#1cfu	2+cfu
(2) Class-10 Ante-chamber	#1cfu	2+cfu.
(3.) CR-2 (Misc)	#1-3cfu	4+cfu.
(4.) CR-1 (Misc)	#1-4cfu	5+cfu

Ⓘⓘ Alert -B " " (Air Sample)   Action -B (Air Sample)

(1.) Class-10 chamber	#1cfu	#2+cfu's
~~(2.) " " Antech~~		
(3) CR-2 (Misc)	#1-2cfu's	#2+cfu's
(4) CR-1 (Misc)	#1-4cfu's	#5+cfu's

Ⓘⓘⓘ Touch Plates   Alert 1cfu   Action 2+cfu.

(*) all = Class-10 chamber

3.03 AH-2   * Add

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 **VERSION NUMBER: ~~2.0~~ 3.0**

Authorized By: Date: 04-06-06 Dept: LAB

Written By: Anne Avezzano Date: 03-28-06

Reviewed By: Date:

Date Effective: OJ 04-06-06

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for non-viable and viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644-4 "Clean Rooms and Associated Controlled Environments, Part 4"

4.4 SOP 1.030 "Deviations ~~– OOS~~"

4.5 SOP 3.010 "Sterile Compounding Area Requirements"

4.6 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.7 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Non-Viable Air Sampler – Device used to provide quantitative analysis of all airborne particles ≥0.5μm in diameter

5.3 Viable Air Sampler – Device used to provide quantitative analysis of viable airborne ~~viable~~

5.4 Surface Contact Plate – Device of known surface area providing a convex surface to remove viable particles from a flat work surface

5.5 ISO Classifications

- 5.5.1 ISO Class [illegible] is equivalent to Class ~~100~~ 10. Glove box Antechamber.
- 5.5.2 ISO Class 6 is equivalent to Class ~~1,000~~
- 5.5.3 ISO Class 7 is equivalent to Class 10,000. Clean Room
- 5.5.4 ISO Class 8 is equivalent to Class 100,000. Anteroom OJ 04-06-06

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⊖ TSA strips

Replace c̄ approp

place

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY	
SOP NUMBER: 3.030	**VERSION NUMBER: 2.0**
Date Effective: DJ 04-06-06	

5.6 ~~Alert Level~~ = Signals a potential drift from normal operating conditions when normal levels of viable/non-viable particulate in a controlled environment are exceeded; reaching alert level does not require investigation. see att

5.7 2 ~~Action Level~~ – Signals a potential drift from normal operating conditions when normal levels of viable/non-viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action see att

Anne

Detailed

Change

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled once per person daily upon completion of sterile compounding and **prior to cleaning**. cleanrooms.

6.2 Surface sampling in the Class 100 (ISO Class 5) area shall be performed weekly upon ~~completion of sterile compounding and~~ **~~prior to~~ cleaning**. Rooms & Boxes &

2 6.3 Sterility of 70% ~~isopropyl~~ alcohol (IPA) will be confirmed weekly.

CHANGED TO WEEKLY 3 6.4 Viable and non-viable air sampling shall be performed at least every six months.

6.5 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

?

~~7.3~~ ~~TSA strips~~ for viable air samplers (if applicable)

7.4 ~~Viable~~ air samplers ~~with sterilized impeller and shroud~~ (BioTest RCS or equivalent) model # Model # SAS Super 180

7.5 Non-viable air sampler (Met One or equivalent) ?

7.6 Appropriate user manuals

7.7 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from "clean" areas to "dirty" areas. ??

9.0 PROCEDURE

Annette

9.1 Upon receipt of commercially prepared TSA contact plates ~~or TSA strips~~, retain the manufacturer's certificate of testing and conformance.

Do we have?

9.2 Verify that the certificate of conformance documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

ADD +

9.3 Document receipt of the media on the Receipt of TSA Strips/Contact Plates form (Attachment 1).

Do We??

9.3.1 Remove two plates from each new lot of media received for positive and negative controls. (Why?)

9.3.2 Label one plate "Positive" and the other plate "Negative," and write the date on each plate.

9.3.3 Do not expose the agar surface of the "Negative" plate. Seal ~~the strip/~~contact plate ~~with a slide seal or tape~~/parafilm.

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DJ 04-06-06

9.3.4 Sample a known "dirty" area for the positive control (bottom of shoe, bare skin, carpet, etc.). Seal the strip/contact plate with a slide seal or tape/parafilm.

9.3.5 Incubate the positive/negative control for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.)

Changed

9.3.6 If the positive control fails (no growth), the lot must be rejected.

~~9.3.7 If the negative control fails (growth), a deviation must be written according to~~ SOP 1.030, "Deviations – OOS."

9.3.8 Place the completed attachment 1, along with the manufacturer's certificates, in a designated binder.

9.3.9 Store all acceptable media according to the manufacturer's recommendation (usually 2°C-8°C) in a monitored refrigerator.

9.4 Non-Viable Air Sampling

9.4.1 Refer to the appropriate Clean Room Facility Air Sampling Log (Attachments 2 and 4).

how?

9.4.2 Verify the air sampler is within calibration and document the manufacturer/model, serial number, and calibration due date on Attachments 2 and 4.

9.4.3 Sanitize the air sampler exterior prior to entry into the clean room facility.

9.4.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.4.5 Prepare the air sampler according to the manufacturer's instructions. The volume of air sampled in all areas will be one cubic foot.

9.4.6 Place the air sampler in the desired location and turn on. **Do not stand over the sampler while in operation.**

10 10

9.4.7 Perform non-viable air sampling beginning in the Class ~~100~~ (ISO Class 5) glove box, ~~followed by the Class 10,000 (ISO Class 7)~~ antechamber, then the Class 10,000 (ISO Class 7) buffer/ preparation room and concluding in the Class 100,000 (ISO Class 8) room.

AR

9.4.8 Record non-viable air sampling results on Attachments 2 and 4, and file all completed documents in the EM binder.

9.5 Viable Air Sampling

9.5.1 Refer to the appropriate Clean Room Facility Air Sampling Log (Attachments 2 and 4).

9.5.2 Obtain the appropriate quantity of media from storage.

  9.5.2.1 Inspect each strip/plate and discard any damaged or contaminated media and replace.

  9.5.2.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 2 and 4.

9.5.3 Verify the air sampler is within calibration and document the manufacturer/model, serial number and calibration due date on Attachments 2 and 4.

9.5.4 Sanitize the air sampler exterior prior to entry into the clean room facility.

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OJ 04-06-06

[illegible] ??

9.5.5 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.5.6 Set up the air sampler according to the manufacturer's instructions.

9.5.7 The volume of air sampled in the Class ~~100~~ 10 (ISO Class ~~5~~ 4) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

9.5.8 Perform viable air sampling beginning in the Class ~~100~~ 10 (ISO Class ~~5~~ 4) glove box, followed by the Class ~~10,000~~ 10 (ISO Class 7) antechamber, then the Class 10,000 (ISO Class 7) ~~buffer/~~ preparation room and concluding in the Class 100,000 (ISO Class 8) room. Anteroom

9.5.8.1 Aseptically remove an agar ~~strip~~/contact plate from its wrapper. Do not touch the agar surface (If agar is touched, discard the strip/contact plate and begin again). ?

are we using plates?

9.5.8.2 ~~If using agar strips, slide the strip into the rotor at the guide plate with the agar surface facing inward until the strip closes the drum slot. If using contact plates/~~ Aseptically remove the cap from the sampler and secure the plate between the metal prongs.

9.5.8.3 Place the air sampler in the desired location and turn on. **Do not stand over the sampler while in operation.**

9.5.8.4 The air sampler will automatically turn off at the conclusion of the sampling period.

9.5.8.5 Aseptically remove the ~~strip~~/contact plate from the sampler. Place the agar strip in its protective cover, or replace the lid of the contact plate.

9.5.8.6 Seal the ~~strip~~/contact plate with ~~a slide seal or tape~~/parafilm.

9.5.8.7 Label the strip with the sample location and document on Attachments 2 and 4.

9.5.9 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. ~~(Samples may be shipped to a contract lab for incubation and analysis.)~~ Document incubation time and temperatures on Attachments 2 and 4 in comments section.

9.5.10 Record viable air sampling results on Attachments 2 and 4, and file all completed documents in the EM binder.

9.6 Surface Sampling

9.6.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 3 and 5).

9.6.2 Surface samples of the Class ~~100~~ 10 (ISO Class ~~5~~ 4) area shall be taken weekly upon completion of sterile compounding and **prior to cleaning**.

9.6.3 Obtain the appropriate quantity of contact plates from storage.

9.6.3.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.6.3.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 3 and 5.

ORIGINAL
09 04-06-06

9.6.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.6.5 Sampling technique:

- 9.6.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Do not touch the agar surface (If agar is touched, discard the plate and begin again). for 10 sec for 10 sec
- 9.6.5.2 Gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface.
- 9.6.5.3 Replace the cover and seal the plate with ~~tape~~/parafilm.
- 9.6.5.4 Record the site location on the base of the plate. Do not record any information on the cover of the plate.
- 9.6.5.5 Clean the sample site per SOP 3.020, "Cleaning and Maintenance of the Clean Room Facility," before proceeding to the next site.

Why do we repeat??

9.6.6 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. ~~(Samples may be shipped to a contract lab for incubation and analysis.)~~ Document incubation times and temperatures on Attachments 3 and 5 in the comments section.

9.6.7 Record surface sampling results on Attachments 3 and 5, and file all completed documents in the EM binder.

9.7 Confirm the Sterility of 70% IPA

9.7.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 3 and 5).

2 random per Clean Room per week as old

9.7.2 Obtain as many contact plates from storage as there are IPA bottles.

- 9.7.2.1 Inspect each plate and discard any damaged or contaminated media and replace.
- 9.7.2.2 Verify media is within expiration dat~~ing~~e, and record media lot number and expiration date on Attachments 3 and 5.

(A)

9.7.3 Aseptically remove the contact plate cover. Do not touch the agar surface (If agar is touched, discard the plate and begin again).

9.7.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.7.5 Replace the cover and seal the plate with ~~tape~~/parafilm.

9.7.6 Label the base of the plate with "IPA" and the IPA lot number/expiration date. Do not record any information on the cover of the plate.

9.7.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. ~~(Samples may be shipped to a contract lab for incubation and analysis.)~~ Document incubation times and temperatures on Attachments 3 and 5.

9.7.8 Record results on Attachments 3 and 5, and file all completed documents in the EM binder.

(*) 9.8 Personnel Monitoring

ORIGINAL
OJ 04-06-06

- White Asked process.
- up to ER personnel.

Data!

→ had to Q.C.O.

9.8.1 Refer to the Clean Room Facility Personnel Touch Plate Log (Attachment 6).

9.8.2 Obtain the appropriate quantity of contact plates from storage.

9.8.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.8.2.2 Verify media is within expiration dat~~ing~~e, and record media lot number and expiration date on Attachment 6.

9.8.3 Record the compounder's name on Attachment 6.

9.8.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.8.5 Replace the cover and seal the plate with ~~tape~~/parafilm.

9.8.6 Label the base of the contact plate with the date, the compounder's initials and the hand sampled.

9.8.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. ~~(Samples may be shipped to a contract lab for incubation and analysis.)~~ Document incubation times and temperatures on Attachment 6.

9.8.8 Record personnel monitoring results on Attachment 6, and file all completed documents in the EM binder.

9.9 **The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.**

9.10 Alert and Action Limits ?

9.10.1 Air Sampling (Viable and ~~Non-Viable~~)

9.10.1.1 Calculate the level of viable airborne particulates as CFU per cubic foot.

9.10.1.2 Calculate the level of non-viable airborne particulates as a quantity of particles ≥0.5μm in diameter per cubic foot.

Proposed levels

9.10.1.3 The alert/action limits for air sampling should be derived from historical data. **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 7).**

9.10.2 Surface and Personnel Monitoring

9.10.2.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.10.2.2 The alert/action limits for surface and personnel monitoring should be derived from historical data. **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 7).**

9.11 Investigation and Corrective Actions

9.11.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

ORIGINAL
04-06-06

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 **VERSION NUMBER: 2.0**

Date Effective: Original 04-06-06

9.11.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized. 3

9.11.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

- 9.11.3.1 Review of sanitation procedures (repeat if necessary)
- 9.11.3.2 Review of sampling technique
- 9.11.3.3 Review of clean room personnel
- 9.11.3.4 Inspection of sampling media

9.11.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

- 9.11.4.1 Identification of microbial isolates to determine origin
- 9.11.4.2 Review of pressure differential information
- 9.11.4.3 Review of HEPA and clean room certification
- 9.11.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.11.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

10.0 ATTACHMENTS

- 10.1 Attachment 1 – Receipt of TSA Strips/Contact Plates
- 10.2 Attachment 2 – Clean Room 1 Air Sampling Log
- 10.3 Attachment 3 – Clean Room 2 Air Sampling Log
- 10.4 Attachment 4 – Clean Room 1 Surface Sampling Log
- 10.5 Attachment 5 – Clean Room 2 Surface Sampling Log
- 10.4 Attachment 6 – Clean Room Facility Personnel Touch Plate Log
- 10.5 Attachment 7 – USP Proposed Levels for Air and Surface Monitoring

11.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP.	CR06012
2.0		Updated section 9.3 and attachment 1 to include positive/negative controls. Updated sample identification labels and schematic maps on attachments 2, 3, 4 and 5.	CR06053

ORIGINAL
OJ 04-06-06

Media type Took out

Correct Terms??

RECEIPT OF ~~TSA STRIPS~~/CONTACT PLATES

Media Type	Manufacturer	Lot Number	Expiration Date	Received By (Initials/Date)	Incubation Dates of Positive and Negative Controls	Positive Control	Negative Control	Result
☐ ~~Strips~~					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ ~~Strips~~					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ ~~Strips~~					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ ~~Strips~~					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ ~~Strips~~					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ ~~Strips~~					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject

Reviewed By: ~~X~~ **Date:**

ORIGINAL
OJ 04-06-06

1

apply ?
Action levels

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATE LOG

Rph/Tech

Media Lot # and Expiration Date	Compounder	Incubation Dates 20°C-25°C (room temperature)	Incubation Dates 30°C-35°C	Results (CFU)	Pass/Fail
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F

R viewed By:

Dat :

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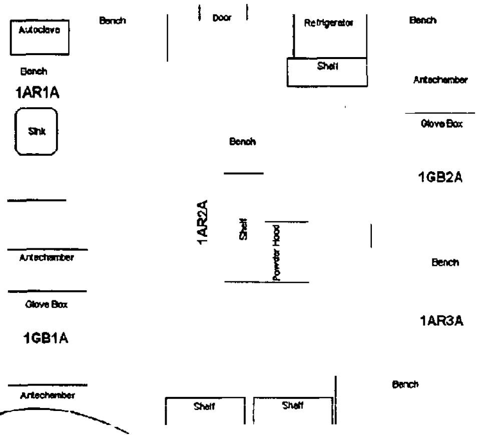
04-06-06

CR-1

CLEAN ROOM 1 AIR SAMPLING LOG



?

		NON-VIABLE SAMPLES		VIABLE SAMPLES		
Sample	Location	Results (Particles/ft³)	Pass/Fail	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
1GB1A	ISO Class ~~5~~ 4 Glove Box	levels	☐P ☐F			☐P ☐F
1GB2A	ISO Class ~~5~~ 4 Glove Box		☐P ☐F			☐P ☐F
1AR1A	ISO Class 7 Room		☐P ☐F			☐P ☐F
1AR2A	ISO Class 7 Room		☐P ☐F			☐P ☐F
1AR3A	ISO Class 7 Room		☐P ☐F			☐P ☐F

Non-Viable Air Sampler
Mfg./Model:
Serial #: Calibration Due:

Viable Air Sampler
Mfg./Model:
Serial #: Calibration Due:
Media Lot #/Expiration Date:

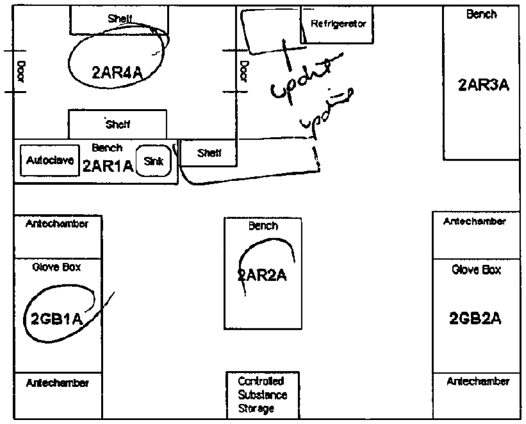
Comments:

Performed By: **Date:**

Reviewed By: **Date:**

ORIGINAL
OJ 04-06-06

CLEAN ROOM 2 AIR SAMPLING LOG



Sample	Location	NON-VIABLE SAMPLES		VIABLE SAMPLES		
	4	Results (Particles/ft^3)	Pass/Fail	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
2GB1A	ISO Class 5 Glove Box 4		☐P ☐F			☐P ☐F
2GB2A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
2AR1A	ISO Class 7 Room		☐P ☐F			☐P ☐F
2AR2A	ISO Class 7 Room		☐P ☐F			☐P ☐F
2AR3A	ISO Class 7 Room		☐P ☐F			☐P ☐F
2AR4A	ISO Class 8 Room Ante		☐P ☐F			☐P ☐F

?

Non-Viable Air Sampler

Mfg./Model: ____________________

Serial #: ____________________ Calibration Due: ____________

?

Viable Air Sampler

Mfg./Model: ____________________

Serial #: ____________________ Calibration Due: ____________

Media Lot #/Expiration Date: ____________________

Comments:

____

____

Performed By: ____________________ **Date:** ____________

Reviewed By: ____________________ **Date:** ____________

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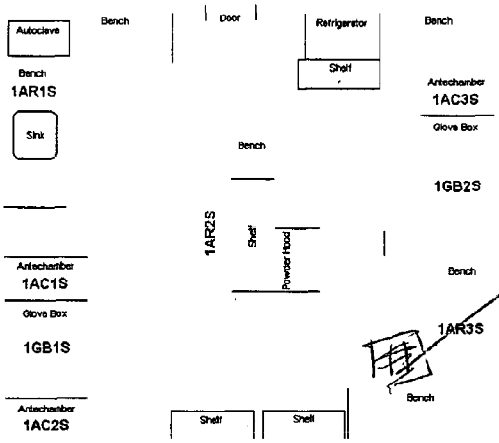
CLEAN ROOM 1 SURFACE SAMPLING LOG



Sample	Location	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
1GB1S	ISO Class ~~5~~ 4 Glove Box			☐P ☐F
1GB2S	ISO Class ~~5~~ 4 Glove Box			☐P ☐F
1AC1S	ISO Class 7 Antechamber			☐P ☐F
1AC2S	ISO Class 7 Antechamber			☐P ☐F
1AC3S	ISO Class 7 Antechamber			☐P ☐F
1AR1S	ISO Class 7 Room			☐P ☐F
1AR2S	ISO Class 7 Room			☐P ☐F
1AR3S	ISO Class 7 Room			☐P ☐F
1IPA	Sterile 70% IPA (+)			☐P ☐F

Media Lot #/Expiration Date:

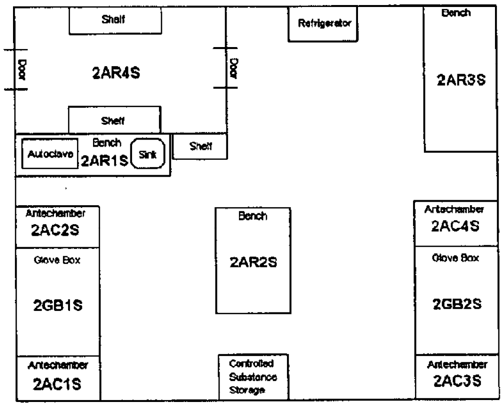
Comments:

Performed By: **Date:**

Reviewed By: **Date:**

ORIGINAL
OJ 04-06-06

CLEAN ROOM 2 SURFACE SAMPLING LOG



Sample	Location	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
2GB1S	ISO Class ~~5~~ 4 Glove Box			☐P ☐F
2GB2S	ISO Class ~~5~~ 4 Glove Box			☐P ☐F
2AC1S	ISO Class 7 Antechamber			☐P ☐F
2AC2S	ISO Class 7 Antechamber			☐P ☐F
2AC3S	ISO Class 7 Antechamber			☐P ☐F
2AC4S	ISO Class 7 Antechamber			☐P ☐F
2AR1S	ISO Class 7 Room			☐P ☐F
2AR2S	ISO Class 7 Room			☐P ☐F
2AR3S	ISO Class 7 Room			☐P ☐F
2AR4S	ISO Class 8 Room (Shelf)			☐P ☐F
2IPA	Sterile 70% IPA ⊕			☐P ☐F

Media Lot #/Expiration Date: ______________________

Comments: ______________________

____

Performed By: ______________________ **Date:** ____________

Reviewed By: ______________________ **Date:** ____________

ORIGINAL
DJ 04-06-06

SOP 3.030 New England Compounding Center Version 2.0

Attachment 5

LEVELS FOR AIR AND SURFACE MONITORING

Note: Alert/Action Levels are to be determined after historical data is collected.

? Levels for Air Sampling

	Classifications	Non-Viable Particles (≥0.5µm/ft³)	Viable Particles (CFU/ft³)	Alert Level	Action Level
Glove box Antechamber	**Critical Areas** Class ~~100~~ 10 (ISO Class ~~5~~) 4	100	< 0.1	N/A ?	N/A ?
	Non-Critical Areas Class ~~1,000~~ – 10,000 (ISO Class ~~6~~ – 7) CR-2/CR-1	~~1,000~~ – 10,000	< 0.5	N/A ?	N/A ?
	Support Areas Class 100,000 Anteroom (ISO Class 8)	100,000	< 2.5	N/A ?	N/A ?

Levels for Surface Sampling

	Classifications	Surface Monitoring (CFU/contact plate)*	Personnel Monitoring (CFU/contact plate)*	Alert Level	Action Level
GB/AC	**Critical Areas** Class ~~100~~ 10 (ISO Class ~~5~~ 4)	3	3 – gloves (5 – mask/gloves)	N/A ?	N/A ?
CR-2 CR-1	**Non-Critical Areas** Class ~~1000~~ – 10,000 (ISO ~~Class 6~~ – 7)	5 (10 including floor)	5 – gloves (10 – mask/gloves)	N/A ?	N/A ?
Anteroom	**Support Areas** Class 100,000 (ISO Class 8)	20 (30 including floor)	15 – gloves (30 – mask/gloves)	N/A ?	N/A ?

(*Contact plate areas vary from 24 to 30 square centimeters. When swabbing is used in sampling, the area covered should be greater than or equal to 24cm^2 but no larger than 30cm^2.)

ORIGINAL
DJ 04-06-06

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER:	**3.030**	**VERSION NUMBER:**	**3.0**
Sterile Laboratory		First Effective Date	**03-28-06**
Originator:		Previous effective Date	04-06-06
Reviewer:		Current Effective Date	

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for non viable and viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644-4 "Clean Rooms and Associated Controlled Environments, Part 4

4.4 SOP 3.010 "Sterile Compounding Area Requirements"

4.5 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.6 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Viable Air Sampler – Device used to provide quantitative analysis of viable airborne ~~viable~~ particles ✓

5.3 Surface Contact Plate – Device of known surface area providing a convex surface to remove viable particles from a flat work surface

5.4 ISO Classifications

- 5.4.1 ISO Class 4 is equivalent to Class 10(Glove box, antechamber).
- 5.4.2 ISO Class 7 is equivalent to Class 10,000(Clean room).
- 5.4.3 ISO Class 8 is equivalent to Class 100,000(Anteroom).

5.5 Alert Level – Signals a potential drift from normal operating conditions when normal levels of viable particulates in a controlled environment are exceeded; reaching alert level does not require investigation. (See Attachment 7)

5.6 Action Level – Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action. (See Attachment 7)

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled once per person daily upon completion of sterile compounding and **prior to cleaning**.

6.2 Surface sampling in the glove boxes and antechambers (ISO Class 4, Class 10), clean room (ISO Class 7 Class 10,000) and anteroom (ISO Class 8 ~~ISO~~ Class 100,000) area shall be performed weekly, **prior to cleaning**.

6.3 Sterility of 70% isopropyl alcohol (IPA) will be confirmed weekly.

6.4 Viable air sampling shall be performed weekly.

6.5 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 Viable air sampler with sterilized impeller and shroud (Model # SAS180)

7.4 Appropriate user manuals

7.5 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from "clean" areas to "dirty" areas.

9.0 PROCEDURE

9.1 Upon receipt of commercially prepared TSA contact plates, retain the manufacturer's certificate of analysis. Document receipt of the media on Receipt of Contact plates (Attachment 1).

9.2 Verify that the certificate of ~~conformance~~ Analysis documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

  9.2.1 Remove two plates from ~~each~~ new lot of media received for positive and negative controls.

  9.2.2 Label one plate "Positive" and the other plate "Negative," and write the date on each plate.

  9.2.3 Do not expose the agar surface of the "Negative" plate. Seal the contact plate with parafilm.

  9.2.4 For the "Positive" control expose the agar to air for 15 minutes. Seal the contact plate with parafilm.

  9.2.5 Incubate the positive/negative control for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. document on Attachment 1.

9.2.6 If the positive (no growth) or negative (growth control fails (no growth/growth), the lot must be rejected.

9.2.7 Place the completed Attachment 1, along with the certificate of analysis, in a designated binder.

9.2.8 Store all acceptable media according to the manufacturer's recommendation (usually 2°C-8°C) in a monitored refrigerator.

9.3 Viable Air Sampling

9.3.1 Refer to the appropriate Clean Room Facility Air Sampling Log (Attachments 2 and 3).

9.3.2 Verify that the air sampler is within calibration and document the manufacturer/model, serial number, and calibration due date on Attachments 2 and 3.

9.3.3 Sanitize the air sampler exterior prior to entry into the clean room facility.

9.3.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.3.5 Obtain the appropriate quantity of media from storage.

9.3.5.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.3.5.2 Verify media is within expiration dat~~ing,~~e and record media lot number and expiration date on Attachments 2 and 3.

9.3.5.3 Aseptically remove an agar contact plate from the package ~~its wrapper~~. Do not touch the agar surface (If agar is touched, discard the contact plate and begin again).

9.3.5.4 ~~If using contact plates a~~Aseptically remove the cap from the sampler and secure the plate between the metal prongs

9.3.6 Set up the air sampler according to the manufacturer's instructions. The volume of air sampled in the Class 10 (ISO Class 4) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

9.3.6.1 Place the viable air sampler in the desired location and turn on. Begin in the Class 10 (ISO Class 4) glove box, followed by the Class 10,000 (ISO Class 7) clean room, then the Class 100,000 (ISO Class 8) anteroom. . **Do not place arms over sampler while in operation.**

9.3.6.2 The air sampler will automatically turn off at the conclusion of the sampling period.

9.3.6.3 Aseptically remove the contact plate from the sampler. Replace the lid of the contact plate.

9.3.6.4 Seal the contact plate with Para film.

9.3.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. ~~(Samples may be shipped to a contract lab for incubation and analysis.)~~ Document Incubation time and temperatures on Attachments 2 and ~~1~~ 3 in ~~comments section~~.

9.3.8 Record viable air sampling results on Attachments 2 and 3, and file all completed documents in the EM binder.

9.4 Surface Sampling

9.4.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 4 and 5).

9.4.2 Surface sampling in the glove boxes and antechambers (ISO Class 4 Class 10), clean room (ISO Class 7 Class 10,000) and anteroom (ISO Class 8 ~~ISO~~ Class 100,000) area shall be performed weekly, **prior to cleaning**

9.4.3 Obtain the appropriate quantity of contact plates from storage.

9.4.3.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.4.3.2 Verify media is within expiration dati~~ng~~e, and record media lot number and expiration date on Attachments 4 and 5.

9.4.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.4.5 Sampling technique:

9.4.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface for 10 seconds.

9.4.5.2 Replace the cover and seal the plate with parafilm.

9.4.5.3 Record the site location on the base of the plate. Do not record any information on the cover of the plate.

9.4.5.4 Clean the sample site with sterile 70% IPA before proceeding to the next site.

9.4.6 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C.

9.4.7 Record surface sampling results on Attachments 4 and 5, and file all completed documents in the EM binder.

9.5 Confirm the Sterility of 70% IPA

9.5.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 4 and 5).

9.5.2 Obtain two contact plates from storage and test two random sterile70% IPA bottles.

9.5.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.5.2.2 Verify media is within expiration date, and record media lot number and expiration date on Attachments 4 and 5.

9.5.3 Aseptically remove the contact plate cover. Do not touch the agar surface (If agar is touched, discard the plate and begin again).

9.5.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.5.5 Replace the cover and seal the plate with parafilm.

9.5.6 Label the base of the plate with "IPA" and the IPA lot number/expiration date. Do not record any information on the cover of the plate.

9.5.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C.

9.5.8 Record results on Attachments 4 and 5, and file all completed documents in the EM binder.

9.6 Personnel Monitoring

9.6.1 Refer to the Clean Room Facility Personnel Touch Plate Log (Attachment 6).

9.6.2 Obtain the appropriate quantity of contact plates from storage.

9.6.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.6.2.2 Verify media is within expiration date.

9.6.2.3 Label the base of the contact plate with the date, the pharmacist/technician initials and the hand sampled.

9.6.2.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.6.3 Replace the cover and seal the plate with parafilm.

9.6.4 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C.

9.6.5 Record personnel monitoring results on Attachment 6 and file all completed documents in the EM binder.

9.7 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

9.8 Alert and Action Limits

9.8.1 Air Sampling (Viable)

9.8.2 Calculate the level of viable airborne particulates as CFU per cubic foot. The volume of air sampled in the Class 10 (ISO Class 4) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

9.8.2.1 The alert/action limits for air sampling should be derived from historical data.* **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring*(Attachment 7).**

9.8.3 Surface and Personnel Monitoring

9.8.3.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.8.3.2 The alert/action limits for surface and personnel monitoring should be derived from historical data.* **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring*(Attachment 7).**

9.9 Investigation and Corrective Actions

9.9.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

9.9.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized.

9.9.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.9.3.1 Review of sanitation procedures ~~(repeat if necessary)~~

9.9.3.2 Review of sampling technique

9.9.3.3 Review of clean room personnel

9.9.3.4 Inspection of sampling media

9.9.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.9.4.1 Identification of microbial isolates to determine origin

9.9.4.2 Review of pressure differential information

9.9.4.3 Review of HEPA and clean room certification

9.9.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.9.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

10.0 ATTACHMENTS

10.1 Attachment 1 – Receipt of Contact Plates

10.2 Attachment 2 – Clean Room 1 Air Sampling Log

10.3 Attachment 3 – Clean Room 2 Air Sampling Log

10.4 Attachment 4 – Clean Room 1 Surface Sampling Log

10.5 Attachment 5 – Clean Room 2 Surface Sampling Log

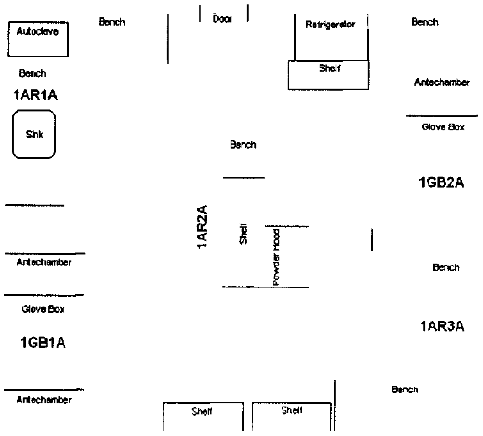
10.4 Attachment 6 – Clean Room Facility Personnel Touch Plate Log

10.5 Attachment 7 – USP Proposed Levels for Air and Surface Monitoring

11.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06012
2.0	04/06/06	Updated section 9.3 and attachment 1 to include positive/negative controls. Updated sample identification labels and schematic maps on attachments 2, 3, 4 and 5.	CR06053
3.0		Taking out TSA Strips, non-viable samples, fixing iso/ classes not correct	CR07018

CLEAN ROOM 1 AIR SAMPLING LOG



VIABLE SAMPLES

Sample	Location	Incubation Dates 20°C-25°C (RT) 30°C-35°C	Results (CFU)	Pass/Fail
1GB1A	ISO Class 4 Glove Box			☐P ☐F
1GB2A	ISO Class 4 Glove Box			☐P ☐F
1AR1A	ISO Class 7 Clean Room			☐P ☐F
1AR2A	ISO Class 7 Clean Room			☐P ☐F
1AR3A	ISO Class 7Clean Room			☐P ☐F

Alert 1 CFU (ISO Class 4 Glove Box)
1-4 CFU (ISO Class 7 Clean Room)

Action 2 CFU (ISO Class 4 Glove Box)
5+ CFU (ISO Class 7 Clean Room)

Viable Air Sampler

Mfg./Model:

Serial #: Calibration Due:

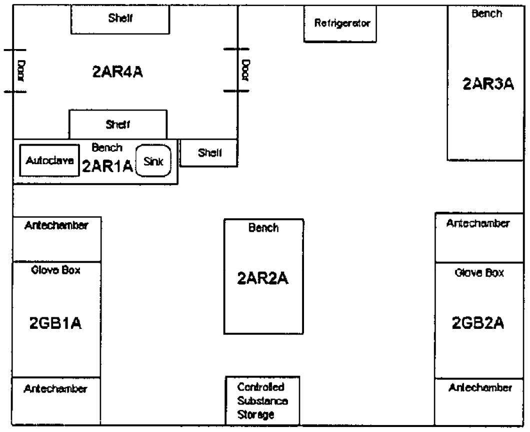
Media Lot #/Expiration Date:

Comments:

Performed By: **Date:**

Reviewed By: **Date:**

CLEAN ROOM 2 AIR SAMPLING LOG



Sample	Location	VIABLE SAMPLES		
		Incubation Dates 20 C - 25 C (RT) 30 C - 35 C	Results (CFU)	Pass/Fail
2GB1A	ISO Class 4 Glove Box			☐P ☐F
2GB2A	ISO Class 4 Glove Box			☐P ☐F
2AR1A	ISO Class 7 Room			☐P ☐F
2AR2A	ISO Class 7 Room			☐P ☐F
2AR3A	ISO Class 7 Room			☐P ☐F
2AR4A	ISO Class 8 Room			☐P ☐F

Alert 1 CFU (ISO Class 4 Glove Box, Antechamber) **Action** 2+ CFU (ISO Class 4 Glove Box, Antechamber)
1-2 CFU (ISO Class 7 Clean Room) 3+ CFU (ISO Class 7 Clean Room)

Viable Air Sampler

Mfg./Model: ______________________

Serial #: ______________________ Calibration Due: ______________

Media Lot #/Expiration Date: ______________________

Comments:

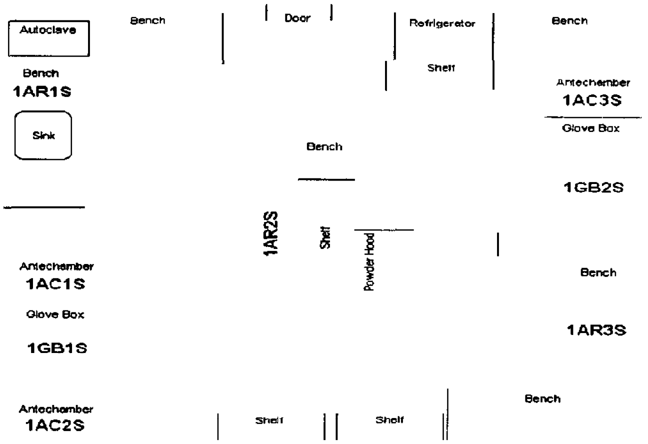
____

____

Performed By: ______________________ **Date:** ______________

Reviewed By: ______________________ **Date:** ______________

CLEAN ROOM 1 SURFACE SAMPLING LOG



Sample	Location	Incubation Dates		Results (CFU)	Pass/Fail
		20°C-25°C(RT)	30°C - 35°C		
1GB1S	ISO Class 4 Glove Box				☐P ☐F
1GB2S	ISO Class 4 Glove Box				☐P ☐F
1AC1S	ISO Class 7 Antechamber				☐P ☐F
1AC2S	ISO Class 7 Antechamber				☐P ☐F
1AC3S	ISO Class 7 Antechamber				☐P ☐F
1AR1S	ISO Class 7 Room				☐P ☐F
1AR2S	ISO Class 7 Room				☐P ☐F
1AR3S	ISO Class 7 Room				☐P ☐F
1IPA1	Sterile 70% IPA				☐P ☐F
1IPA2	Sterile 70% IPA				☐P ☐F

Alert 1 CFU (ISO Class 4 Glove Box, Antechamber)
1-4CFU (ISO Class 7 Clean Room)

Action 2+ CFU (ISO Class 4 Glove Box, Antechamber)
5+ CFU (ISO Class 7 Clean Room)

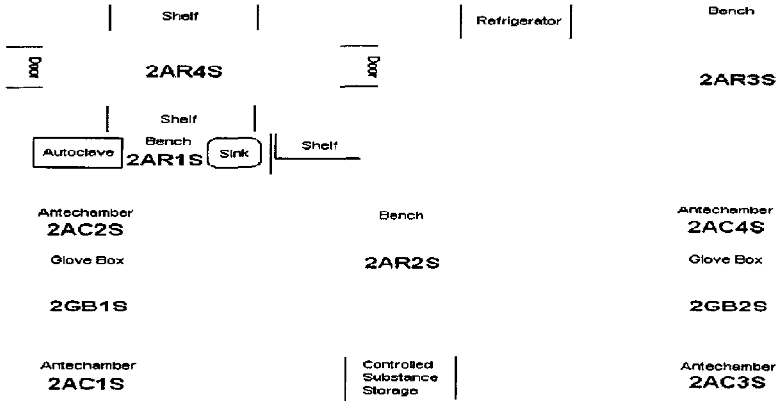
Media Lot #/Expiration Date:

Comments:

Performed By: **Date:**

Reviewed By: **Date:**

CLEAN ROOM 2 SURFACE SAMPLING LOG



Sample	Location	20°C-25°C (RT) Incubation Dates	30°C-35°C Results (CFU)	Pass/Fail
2GB1S	ISO Class 4 Glove Box			☐P ☐F
2GB2S	ISO Class 4 Glove Box			☐P ☐F
2AC1S	ISO Class 7 Antechamber			☐P ☐F
2AC2S	ISO Class 7 Antechamber			☐P ☐F
2AC3S	ISO Class 7 Antechamber			☐P ☐F
2AC4S	ISO Class 7 Antechamber			☐P ☐F
2AR1S	ISO Class 7 Room			☐P ☐F
2AR2S	ISO Class 7 Room			☐P ☐F
2AR3S	ISO Class 7 Room			☐P ☐F
2AR4S	ISO Class 8 Room (Shelf)			☐P ☐F
2IPA1	Sterile 70% IPA			☐P ☐F
2IPA2	Sterile 70% IPA			☐P ☐F

Alert 1 CFU (ISO Class 4 Glove Box, Antechamber) **Action** 2+ CFU (ISO Class 4 Glove Box, Antechamber)
1-3CFU (ISO Class 7 Clean Room) 4+ CFU (ISO Class 7 Clean Room)

Media Lot #/Expiration Date:

Comments:

Performed By: **Date:**

Reviewed By: **Date:**

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATE LOG

Media Lot # and Expiration Date	Rph / Tech	Incubation Dates 20°C-25°C (room temperature)	Incubation Dates 30°C-35°C	Results (CFU)	Pass/Fail
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F

Alert Level **1 CFU**

Action Level **2+ CFU**

Reviewed By:

Date:

RECEIPT OF CONTACT PLATES

Manufacturer	Lot Number	Expiration Date	Received By (Initials/Date)	Incubation Dates of Positive and Negative Controls	Positive Control	Negative Control	Result
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
				20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
				30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject

Performed By: **Date:**

Reviewed By: **Date:**

LEVELS FOR AIR AND SURFACE MONITORING

Note: Alert/Action Levels are to be determined after historical data is collected.

Levels for Air Sampling

Classifications	**Viable Particles (CFU/ft^3)**	**Alert Level**	**Action Level**
Critical Areas Class 10 ISO Class 4) (glove box, antechamber)	< 0.1	**CR1/CR2 1 CFU**	**CR1/CR2 2+ CFU**
Non-Critical Areas Class 10,000 (ISO Class 7) (clean room)	< 0.5	**CR1 1-4 CFU** **CR2 1-2 CFU**	**CR1 5+ CFU** **CR2 3+ CFU**
Support Areas Class 100,000 (ISO Class 8)(anteroom)	< 2.5	**CR2 1-3N/A**	**CR2 4+CFU**

Levels for Surface Sampling

Classifications	**Surface Monitoring (CFU/contact plate)***	**Personnel Monitoring (CFU/contact plate)***	**Alert Level**	**Action Level**
Critical Areas Class 10 (ISO Class 4)	3	3 – gloves (5 – mask/gloves)	**CR1/CR2 1CFU**	**2+ CFU**
Non-Critical Areas Class 10,000 (ISO Class 7)	5 (10 including floor)	5 – gloves (10 – mask/gloves)	**CR1 1-4CFU** **CR2 1-3CFU**	**5+ CFU** **4+ CFU**
Support Areas Class 100,000 (ISO Class 8)	20 (30 including floor)	15 – gloves (30 – mask/gloves)	**CR2 1-3CFU**	**4+CFU**

*Contact plate areas vary from 24 to 30 square centimeters.

SOP REVIEW FORM

(Page 2 of 2)

SOP Number/Title: 3.030
Environmental Monitoring of the Clean Room Facility

Date Effective: 03-08-06 **Version:** 2.0 **Last Reviewed:** 03-08-07

SOP REVIEW – PLEASE CHECK THE FOLLOWING AS THEY ARE PERFORMED:

- ☑ Ensure that the purpose, scope, responsibilities, definitions, and general information sections are still accurate and current.
- ☑ Ensure that the responsible functional area groups are consistent with current organizational structure.
- ☑ Check references to ensure that they still apply, that the titles have not changed, and that the references to documents within the text are correct.
- ☑ Verify that all materials, equipment, reagents, etc. called for in the procedure are still available and are being used.
- ☑ Ensure that the current practice is reflected accurately in the procedure section of the SOP.
- ☑ Ensure that the procedure addresses what action to take if the task has unacceptable results.
- ☑ Ensure that all documentation requirements and storage/archival requirements are reflected in the SOP.
- ☑ Ensure that all attachments continue to be accurate and reflect current practices.

CHOOSE THE STATEMENT THAT APPLIES:

I have reviewed the above mentioned procedure and:

- ☑ No changes need to be implemented.
- ☐ SOP Change Request is attached to update the procedure, Change Request Log Number CR______________.
- ☐ SOP should be obsoleted, Change Request Log Number CR______________.

SOP Review Performed By: Annette M. Robinson **Date:** 08-31-07

ORIGINAL
AA 03-07-06

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 **VERSION NUMBER: 2.0**

Authorized By: Date: 04-06-06 Dept: LAB

Written By: Anne Avezzano Date: 03-28-06

Reviewed By: Date:

Date Effective: OJ 04-06-06

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for non-viable and viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644-4 "Clean Rooms and Associated Controlled Environments, Part 4"

4.4 SOP 1.030 "Deviations – OOS"

4.5 SOP 3.010 "Sterile Compounding Area Requirements"

4.6 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.7 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Non-Viable Air Sampler – Device used to provide quantitative analysis of all airborne particles ≥0.5μm in diameter

5.3 Viable Air Sampler – Device used to provide quantitative analysis of viable airborne viable

5.4 Surface Contact Plate – Device of known surface area providing a convex surface to remove viable particles from a flat work surface

5.5 ISO Classifications

5.5.1 ISO Class 5 is equivalent to Class 100.

5.5.2 ISO Class 6 is equivalent to Class 1,000.

5.5.3 ISO Class 7 is equivalent to Class 10,000.

5.5.4 ISO Class 8 is equivalent to Class 100,000.

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5.6 Alert Level – Signals a potential drift from normal operating conditions when normal levels of viable/non-viable particulate in a controlled environment are exceeded; reaching alert level does not require investigation

5.7 Action Level – Signals a potential drift from normal operating conditions when normal levels of viable/non-viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled once per person daily upon completion of sterile compounding and **prior to cleaning.**

6.2 Surface sampling in the Class 100 (ISO Class 5) area shall be performed weekly upon completion of sterile compounding and **prior to cleaning**.

6.3 Sterility of 70% isopropyl alcohol (IPA) will be confirmed weekly.

6.4 Viable and non-viable air sampling shall be performed at least every six months.

6.5 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 TSA strips for viable air samplers (if applicable)

7.4 Viable air samplers with sterilized impeller and shroud (BioTest RCS or equivalent)

7.5 Non-viable air sampler (Met One or equivalent)

7.6 Appropriate user manuals

7.7 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from "clean" areas to "dirty" areas.

9.0 PROCEDURE

9.1 Upon receipt of commercially prepared TSA contact plates or TSA strips, retain the manufacturer's certificate of testing and conformance.

9.2 Verify that the certificate of conformance documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

9.3 Document receipt of the media on the Receipt of TSA Strips/Contact Plates form (Attachment 1).

9.3.1 Remove two plates from each new lot of media received for positive and negative controls.

9.3.2 Label one plate "Positive" and the other plate "Negative," and write the date on each plate.

9.3.3 Do not expose the agar surface of the "Negative" plate. Seal the strip/contact plate with a slide seal or tape/parafilm.

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9.3.4 Sample a known "dirty" area for the positive control (bottom of shoe, bare skin, carpet, etc.). Seal the strip/contact plate with a slide seal or tape/parafilm.

9.3.5 Incubate the positive/negative control for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.)

9.3.6 If the positive control fails (no growth), the lot must be rejected.

9.3.7 If the negative control fails (growth), a deviation must be written according to SOP 1.030, "Deviations – OOS."

9.3.8 Place the completed attachment 1, along with the manufacturer's certificates, in a designated binder.

9.3.9 Store all acceptable media according to the manufacturer's recommendation (usually 2°C-8°C) in a monitored refrigerator.

9.4 Non-Viable Air Sampling

9.4.1 Refer to the appropriate Clean Room Facility Air Sampling Log (Attachments 2 and 4).

9.4.2 Verify the air sampler is within calibration and document the manufacturer/model, serial number, and calibration due date on Attachments 2 and 4.

9.4.3 Sanitize the air sampler exterior prior to entry into the clean room facility.

9.4.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.4.5 Prepare the air sampler according to the manufacturer's instructions. The volume of air sampled in all areas will be one cubic foot.

9.4.6 Place the air sampler in the desired location and turn on. **Do not stand over the sampler while in operation.**

9.4.7 Perform non-viable air sampling beginning in the Class 100 (ISO Class 5) glove box, followed by the Class 10,000 (ISO Class 7) antechamber, then the Class 10,000 (ISO Class 7) buffer/ preparation room and concluding in the Class 100,000 (ISO Class 8) room.

9.4.8 Record non-viable air sampling results on Attachments 2 and 4, and file all completed documents in the EM binder.

9.5 Viable Air Sampling

9.5.1 Refer to the appropriate Clean Room Facility Air Sampling Log (Attachments 2 and 4).

9.5.2 Obtain the appropriate quantity of media from storage.

9.5.2.1 Inspect each strip/plate and discard any damaged or contaminated media and replace.

9.5.2.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 2 and 4.

9.5.3 Verify the air sampler is within calibration and document the manufacturer/model, serial number and calibration due date on Attachments 2 and 4.

9.5.4 Sanitize the air sampler exterior prior to entry into the clean room facility.

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9.5.5 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.5.6 Set up the air sampler according to the manufacturer's instructions.

9.5.7 The volume of air sampled in the Class 100 (ISO Class 5) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

9.5.8 Perform viable air sampling beginning in the Class 100 (ISO Class 5) glove box, followed by the Class 10,000 (ISO Class 7) antechamber, then the Class 10,000 (ISO Class 7) buffer/ preparation room and concluding in the Class 100,000 (ISO Class 8) room.

- 9.5.8.1 Aseptically remove an agar strip/contact plate from its wrapper. Do not touch the agar surface (If agar is touched, discard the strip/contact plate and begin again).
- 9.5.8.2 If using agar strips, slide the strip into the rotor at the guide plate with the agar surface facing inward until the strip closes the drum slot. If using contact plates aseptically remove the cap from the sampler and secure the plate between the metal prongs.
- 9.5.8.3 Place the air sampler in the desired location and turn on. **Do not stand over the sampler while in operation.**
- 9.5.8.4 The air sampler will automatically turn off at the conclusion of the sampling period.
- 9.5.8.5 Aseptically remove the strip/contact plate from the sampler. Place the agar strip in its protective cover, or replace the lid of the contact plate.
- 9.5.8.6 Seal the strip/contact plate with a slide seal or tape/parafilm.
- 9.5.8.7 Label the strip with the sample location and document on Attachments 2 and 4.

9.5.9 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation time and temperatures on Attachments 2 and 4 in comments section.

9.5.10 Record viable air sampling results on Attachments 2 and 4, and file all completed documents in the EM binder.

9.6 Surface Sampling

9.6.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 3 and 5).

9.6.2 Surface samples of the Class 100 (ISO Class 5) area shall be taken weekly upon completion of sterile compounding and **prior to cleaning**.

9.6.3 Obtain the appropriate quantity of contact plates from storage.

- 9.6.3.1 Inspect each plate and discard any damaged or contaminated media and replace.
- 9.6.3.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 3 and 5.

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09 04-06-06

9.6.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.6.5 Sampling technique:

9.6.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Do not touch the agar surface (If agar is touched, discard the plate and begin again).

9.6.5.2 Gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface.

9.6.5.3 Replace the cover and seal the plate with tape/parafilm.

9.6.5.4 Record the site location on the base of the plate. Do not record any information on the cover of the plate.

9.6.5.5 Clean the sample site per SOP 3.020, "Cleaning and Maintenance of the Clean Room Facility," before proceeding to the next site.

9.6.6 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation times and temperatures on Attachments 3 and 5 in the comments section.

9.6.7 Record surface sampling results on Attachments 3 and 5, and file all completed documents in the EM binder.

9.7 Confirm the Sterility of 70% IPA

9.7.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 3 and 5).

9.7.2 Obtain as many contact plates from storage as there are IPA bottles.

9.7.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.7.2.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 3 and 5.

9.7.3 Aseptically remove the contact plate cover. Do not touch the agar surface (If agar is touched, discard the plate and begin again).

9.7.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.7.5 Replace the cover and seal the plate with tape/parafilm.

9.7.6 Label the base of the plate with "IPA" and the IPA lot number/expiration date. Do not record any information on the cover of the plate.

9.7.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation times and temperatures on Attachments 3 and 5.

9.7.8 Record results on Attachments 3 and 5, and file all completed documents in the EM binder.

9.8 Personnel Monitoring

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OJ 04-06 06

9.8.1 Refer to the Clean Room Facility Personnel Touch Plate Log (Attachment 6).

9.8.2 Obtain the appropriate quantity of contact plates from storage.

9.8.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.8.2.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachment 6.

9.8.3 Record the compounder's name on Attachment 6.

9.8.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.8.5 Replace the cover and seal the plate with tape/parafilm.

9.8.6 Label the base of the contact plate with the date, the compounder's initials and the hand sampled.

9.8.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation times and temperatures on Attachment 6.

9.8.8 Record personnel monitoring results on Attachment 6, and file all completed documents in the EM binder.

9.9 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

9.10 Alert and Action Limits

9.10.1 Air Sampling (Viable and Non-Viable)

9.10.1.1 Calculate the level of viable airborne particulates as CFU per cubic foot.

9.10.1.2 Calculate the level of non-viable airborne particulates as a quantity of particles ≥0.5μm in diameter per cubic foot.

9.10.1.3 The alert/action limits for air sampling should be derived from historical data. **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 7).**

9.10.2 Surface and Personnel Monitoring

9.10.2.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.10.2.2 The alert/action limits for surface and personnel monitoring should be derived from historical data. **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 7).**

9.11 Investigation and Corrective Actions

9.11.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

ORIGINAL
04-06-06

9.11.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized.

9.11.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.11.3.1 Review of sanitation procedures (repeat if necessary)

9.11.3.2 Review of sampling technique

9.11.3.3 Review of clean room personnel

9.11.3.4 Inspection of sampling media

9.11.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.11.4.1 Identification of microbial isolates to determine origin

9.11.4.2 Review of pressure differential information

9.11.4.3 Review of HEPA and clean room certification

9.11.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.11.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

10.0 ATTACHMENTS

10.1 Attachment 1 – Receipt of TSA Strips/Contact Plates

10.2 Attachment 2 – Clean Room 1 Air Sampling Log

10.3 Attachment 3 – Clean Room 2 Air Sampling Log

10.4 Attachment 4 – Clean Room 1 Surface Sampling Log

10.5 Attachment 5 – Clean Room 2 Surface Sampling Log

10.4 Attachment 6 – Clean Room Facility Personnel Touch Plate Log

10.5 Attachment 7 – USP Proposed Levels for Air and Surface Monitoring

11.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP.	CR06012
2.0		Updated section 9.3 and attachment 1 to include positive/negative controls. Updated sample identification labels and schematic maps on attachments 2, 3, 4 and 5.	CR06053

ORIGINAL
DJ 04-06-06

SOP CHANGE REQUEST

(Page 1 of 2)

Check one: ☐ New ☑ Change **Change Request Log Number:** CR06053

SOP Number/Title: 3.030, Environmental Monitoring of the Clean Room Facility

Version of SOP being changed: 1.0 **New Version:** 2.0

Description/Text of Change: (see attached Changed Document)
Added procedure for positive/negative controls for media and updated sample identification labels and schematic maps on attachments 2,3,4 and 5

Reason for Change Request:
Original SOP did not include procedure for positive/negative controls for media, and sample identification labels were conflicting.

Supporting Documentation: (mark one)

☑ None Required ☐ Attached → reference (specify): ____________

Requested Implementation Date: (mark one)

☑ Less than 30 Days ☐ By Date: ____________

Annual SOP Review Requirements: (mark one)

☐ Complete review was performed to satisfy the requirements of SOP review (see page 2).

☑ Review limited to changes only, SOP review will need to be performed when scheduled.

Check Training Requirements: (mark one)

☑ Read and Understand Memo ☐ Training Session Required

Training Checklist:

☑ No Checklist is Required **OR** TC#__________ has been reviewed and:

☐ No Changes are Required

☐ Checklist needs to be Written/Changes are Required → TC change # ____________

Change Originator:	Anne Avezzano Printed Name	Signature	03-27-06 Date
Quality Control:	Dan Jayal Printed Name	D. Jayal Signature	03-27-06 Date

ORIGINAL
AA 03-07-06

SOP REVIEW FORM

(Page 2 of 2)

SOP Number/Title:

Date Effective: **Version:** **Last Reviewed:**

SOP REVIEW – PLEASE CHECK THE FOLLOWING AS THEY ARE PERFORMED:

☐ Ensure that the purpose, scope, responsibilities, definitions, and general information sections are still accurate and current.

☐ Ensure that the responsible functional area groups are consistent with current organizational structure.

☐ Check references to ensure that they still apply, that the titles have not changed, and that the references to documents within the text are correct.

☐ Verify that all materials, equipment, reagents, etc. called for in the procedure are still available and are being used.

☐ Ensure that the current practice is reflected accurately in the procedure section of the SOP.

☐ Ensure that the procedure addresses what action to take if the task has unacceptable results.

☐ Ensure that all documentation requirements and storage/archival requirements are reflected in the SOP.

☐ Ensure that all attachments continue to be accurate and reflect current practices.

N/A AA 03-08-06

CHOOSE THE STATEMENT THAT APPLIES:

I have reviewed the above mentioned procedure and:

☐ No changes need to be implemented.

☐ SOP Change Request is attached to update the procedure, Change Request Log Number CR

☐ SOP should be obsoleted, Change Request Log Number CR

SOP Review Performed By: **Date:**

ORIGINAL
AA 03-09-06

RECEIPT OF TSA STRIPS/CONTACT PLATES

M dia Type	Manufacturer	Lot Number	Expiration Date	Received By (Initials/Date)	Incubation Dates of Positive and Negative Controls	Positive Control	Negative Control	Result
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject

Reviewed By:

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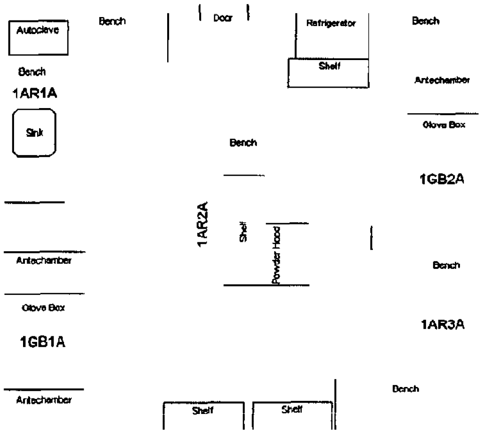
0J 04-06-04

CLEAN ROOM 1 AIR SAMPLING LOG



		NON-VIABLE SAMPLES		VIABLE SAMPLES		
Sample	**Location**	**Results (Particles/ft^3)**	**Pass/Fail**	**Incubation Dates (If Applicable)**	**Results (CFU)**	**Pass/Fail**
1GB1A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
1GB2A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
1AR1A	ISO Class 7 Room		☐P ☐F			☐P ☐F
1AR2A	ISO Class 7 Room		☐P ☐F			☐P ☐F
1AR3A	ISO Class 7 Room		☐P ☐F			☐P ☐F

Non-Viable Air Sampler

Mfg./Model:

Serial #: Calibration Due:

Viable Air Sampler

Mfg./Model:

Serial #: Calibration Due:

Media Lot #/Expiration Date:

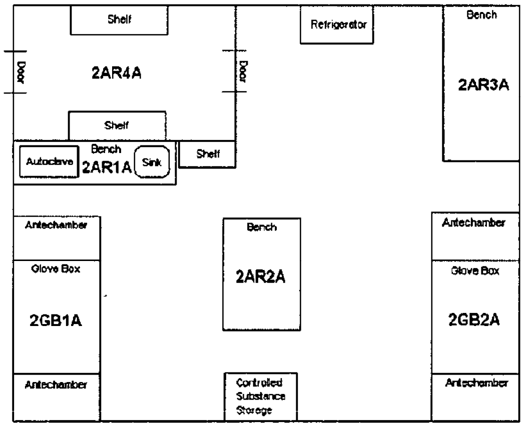
Comments:

Performed By: **Date:**

Reviewed By: **Date:**

ORIGINAL
OJ 04-06-06

CLEAN ROOM 2 AIR SAMPLING LOG



Sample	Location	NON-VIABLE SAMPLES		VIABLE SAMPLES		
		Results (Particles/ft^3)	Pass/Fail	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
2GB1A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
2GB2A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
2AR1A	ISO Class 7 Room		☐P ☐F			☐P ☐F
2AR2A	ISO Class 7 Room		☐P ☐F			☐P ☐F
2AR3A	ISO Class 7 Room		☐P ☐F			☐P ☐F
2AR4A	ISO Class 8 Room		☐P ☐F			☐P ☐F

Non-Viable Air Sampler

Mfg./Model: ______________________________

Serial #: ______________________________ Calibration Due: ____________

Viable Air Sampler

Mfg./Model: ______________________________

Serial #: ______________________________ Calibration Due: ____________

Media Lot #/Expiration Date: ______________________________

Comments:

____

____

Performed By: ______________________________ **Date:** ____________

Reviewed By: ______________________________ **Date:** ____________

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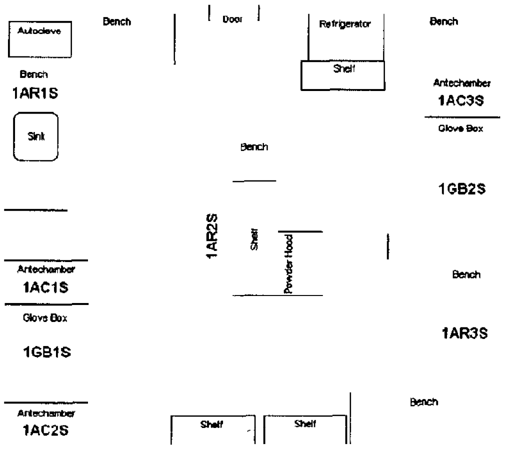
CLEAN ROOM 1 SURFACE SAMPLING LOG



Sample	Location	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
1GB1S	ISO Class 5 Glove Box			☐P ☐F
1GB2S	ISO Class 5 Glove Box			☐P ☐F
1AC1S	ISO Class 7 Antechamber			☐P ☐F
1AC2S	ISO Class 7 Antechamber			☐P ☐F
1AC3S	ISO Class 7 Antechamber			☐P ☐F
1AR1S	ISO Class 7 Room			☐P ☐F
1AR2S	ISO Class 7 Room			☐P ☐F
1AR3S	ISO Class 7 Room			☐P ☐F
1IPA	Sterile 70% IPA			☐P ☐F

Media Lot #/Expiration Date:

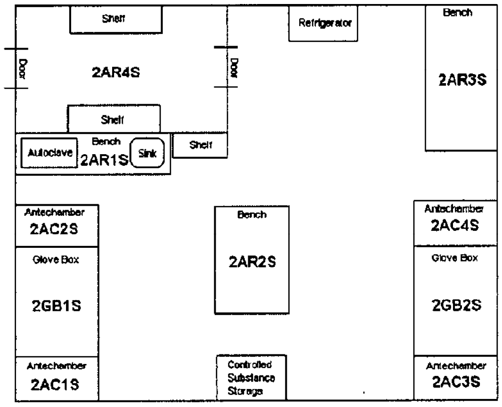
Comments:

Performed By: **Date:**

Reviewed By: **Date:**

ORIGINAL
OJ 04-06-06

CLEAN ROOM 2 SURFACE SAMPLING LOG



Sample	Location	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
2GB1S	ISO Class 5 Glove Box			☐P ☐F
2GB2S	ISO Class 5 Glove Box			☐P ☐F
2AC1S	ISO Class 7 Antechamber			☐P ☐F
2AC2S	ISO Class 7 Antechamber			☐P ☐F
2AC3S	ISO Class 7 Antechamber			☐P ☐F
2AC4S	ISO Class 7 Antechamber			☐P ☐F
2AR1S	ISO Class 7 Room			☐P ☐F
2AR2S	ISO Class 7 Room			☐P ☐F
2AR3S	ISO Class 7 Room			☐P ☐F
2AR4S	ISO Class 8 Room (Shelf)			☐P ☐F
2IPA	Sterile 70% IPA			☐P ☐F

Media Lot #/Expiration Date: ____________________

Comments:

____

____

Performed By: ____________________ **Date:** __________

Reviewed By: ____________________ **Date:** __________

ORIGINAL
DJ 04-06-06

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATE LOG

Media Lot # and Expiration Date	Compounder	Incubation Dates 20°C-25°C (room temperature)	Incubation Dates 30°C-35°C	Results (CFU)	Pass/Fail
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F

Reviewed By:

Date:

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04-06-06

LEVELS FOR AIR AND SURFACE MONITORING

Note: Alert/Action Levels are to be determined after historical data is collected.

Levels for Air Sampling

Classifications	Non-Viable Particles ($\geq 0.5\mu m/ft^3$)	Viable Particles (CFU/ft^3)	Alert Level	Action Level
Critical Areas Class 100 (ISO Class 5)	100	< 0.1	**N/A**	**N/A**
Non-Critical Areas Class 1,000 – 10,000 (ISO Class 6 – 7)	1,000 – 10,000	< 0.5	**N/A**	**N/A**
Support Areas Class 100,000 (ISO Class 8)	100,000	< 2.5	**N/A**	**N/A**

Levels for Surface Sampling

Classifications	Surface Monitoring (CFU/contact plate)*	Personnel Monitoring (CFU/contact plate)*	Alert Level	Action Level
Critical Areas Class 100 (ISO Class 5)	3	3 – gloves (5 – mask/gloves)	**N/A**	**N/A**
Non-Critical Areas Class 1,000 – 10,000 (ISO Class 6 – 7)	5 (10 including floor)	5 – gloves (10 – mask/gloves)	**N/A**	**N/A**
Support Areas Class 100,000 (ISO Class 8)	20 (30 including floor)	15 – gloves (30 – mask/gloves)	**N/A**	**N/A**

(*Contact plate areas vary from 24 to 30 square centimeters. When swabbing is used in sampling, the area covered should be greater than or equal to $24cm^2$ but no larger than $30cm^2$.)

ORIGINAL
OJ 04-06-06

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY		
SOP NUMBER: 3.030	**VERSION NUMBER: 2.0**	
Authorized By:	Date:	Dept: LAB
Written By: Anne Avezzano	Date: 03-28-06	
Reviewed By:	Date:	
Date Effective:		

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1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for non-viable and viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644-4 "Clean Rooms and Associated Controlled Environments, Part 4"

4.4 SOP 1.030 "Deviations – OOS"

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4.5 SOP 3.010 "Sterile Compounding Area Requirements"

4.6 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.7 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Non-Viable Air Sampler – Device used to provide quantitative analysis of all airborne particles ≥0.5μm in diameter

5.3 Viable Air Sampler – Device used to provide quantitative analysis of viable airborne viable

5.4 Surface Contact Plate – Device of known surface area providing a convex surface to remove viable particles from a flat work surface

5.5 ISO Classifications

- 5.5.1 ISO Class 5 is equivalent to Class 100.
- 5.5.2 ISO Class 6 is equivalent to Class 1,000.
- 5.5.3 ISO Class 7 is equivalent to Class 10,000.
- 5.5.4 ISO Class 8 is equivalent to Class 100,000.

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5.6 Alert Level – Signals a potential drift from normal operating conditions when normal levels of viable/non-viable particulate in a controlled environment are exceeded; reaching alert level does not require investigation

5.7 Action Level – Signals a potential drift from normal operating conditions when normal levels of viable/non-viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled once per person daily upon completion of sterile compounding and **prior to cleaning**.

6.2 Surface sampling in the Class 100 (ISO Class 5) area shall be performed weekly upon completion of sterile compounding and **prior to cleaning**.

6.3 Sterility of 70% isopropyl alcohol (IPA) will be confirmed weekly.

6.4 Viable and non-viable air sampling shall be performed at least every six months.

6.5 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 TSA strips for viable air samplers (if applicable)

7.4 Viable air samplers with sterilized impeller and shroud (BioTest RCS or equivalent)

7.5 Non-viable air sampler (Met One or equivalent)

7.6 Appropriate user manuals

7.7 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from "clean" areas to "dirty" areas.

9.0 PROCEDURE

9.1 Upon receipt of commercially prepared TSA contact plates or TSA strips, retain the manufacturer's certificate of testing and conformance.

9.2 Verify that the certificate of conformance documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

9.3 Document receipt of the media on the Receipt of TSA Strips/Contact Plates form (Attachment 1).

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- 9.3.1 Remove two plates from each new lot of media received for positive and negative controls.
- 9.3.2 Label one plate "Positive" and the other plate "Negative," and write the date on each plate
- 9.3.3 Do not expose the agar surface of the "Negative" plate. Seal the strip/contact plate with a slide seal or tape/parafilm.

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9.3.4 Sample a known "dirty" area for the positive control (bottom of shoe, bare skin, carpet, etc.). Seal the strip/contact plate with a slide seal or tape/parafilm.

9.3.5 Incubate the positive/negative control for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.)

9.3.6 If the positive control fails (no growth), the lot must be rejected.

9.3.7 If the negative control fails (growth), a deviation must be written according to SOP 1.030, "Deviations – OOS."

9.3.8 Place the completed attachment 1, along with the manufacturer's certificates, in a designated binder.

9.3.9 Store all acceptable media according to the manufacturer's recommendation (usually 2°C-8°C) in a monitored refrigerator.

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9.4 Non-Viable Air Sampling

9.4.1 Refer to the appropriate Clean Room Facility Air Sampling Log (Attachments 2 and 4).

9.4.2 Verify the air sampler is within calibration and document the manufacturer/model, serial number, and calibration due date on Attachments 2 and 4.

9.4.3 Sanitize the air sampler exterior prior to entry into the clean room facility.

9.4.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.4.5 Prepare the air sampler according to the manufacturer's instructions. The volume of air sampled in all areas will be one cubic foot.

9.4.6 Place the air sampler in the desired location and turn on. **Do not stand over the sampler while in operation.**

9.4.7 Perform non-viable air sampling beginning in the Class 100 (ISO Class 5) glove box, followed by the Class 10,000 (ISO Class 7) antechamber, then the Class 10,000 (ISO Class 7) buffer/ preparation room and concluding in the Class 100,000 (ISO Class 8) room.

9.4.8 Record non-viable air sampling results on Attachments 2 and 4, and file all completed documents in the EM binder.

9.5 Viable Air Sampling

9.5.1 Refer to the appropriate Clean Room Facility Air Sampling Log (Attachments 2 and 4).

9.5.2 Obtain the appropriate quantity of media from storage.

9.5.2.1 Inspect each strip/plate and discard any damaged or contaminated media and replace.

9.5.2.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 2 and 4.

9.5.3 Verify the air sampler is within calibration and document the manufacturer/model, serial number and calibration due date on Attachments 2 and 4.

9.5.4 Sanitize the air sampler exterior prior to entry into the clean room facility.

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9.5.5 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.5.6 Set up the air sampler according to the manufacturer's instructions.

9.5.7 The volume of air sampled in the Class 100 (ISO Class 5) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

9.5.8 Perform viable air sampling beginning in the Class 100 (ISO Class 5) glove box, followed by the Class 10,000 (ISO Class 7) antechamber, then the Class 10,000 (ISO Class 7) buffer/ preparation room and concluding in the Class 100,000 (ISO Class 8) room.

9.5.8.1 Aseptically remove an agar strip/contact plate from its wrapper. Do not touch the agar surface (If agar is touched, discard the strip/contact plate and begin again).

9.5.8.2 If using agar strips, slide the strip into the rotor at the guide plate with the agar surface facing inward until the strip closes the drum slot. If using contact plates aseptically remove the cap from the sampler and secure the plate between the metal prongs.

9.5.8.3 Place the air sampler in the desired location and turn on. **Do not stand over the sampler while in operation.**

9.5.8.4 The air sampler will automatically turn off at the conclusion of the sampling period.

9.5.8.5 Aseptically remove the strip/contact plate from the sampler. Place the agar strip in its protective cover, or replace the lid of the contact plate.

9.5.8.6 Seal the strip/contact plate with a slide seal or tape/parafilm.

9.5.8.7 Label the strip with the sample location and document on Attachments 2 and 4.

9.5.9 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation time and temperatures on Attachments 2 and 4 in comments section.

9.5.10 Record viable air sampling results on Attachments 2 and 4, and file all completed documents in the EM binder.

9.6 Surface Sampling

9.6.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 3 and 5).

9.6.2 Surface samples of the Class 100 (ISO Class 5) area shall be taken weekly upon completion of sterile compounding and **prior to cleaning**.

9.6.3 Obtain the appropriate quantity of contact plates from storage.

9.6.3.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.6.3.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 3 and 5.

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9.6.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.6.5 Sampling technique:

9.6.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Do not touch the agar surface (If agar is touched, discard the plate and begin again).

9.6.5.2 Gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface.

9.6.5.3 Replace the cover and seal the plate with tape/parafilm.

9.6.5.4 Record the site location on the base of the plate. Do not record any information on the cover of the plate.

9.6.5.5 Clean the sample site per SOP 3.020, "Cleaning and Maintenance of the Clean Room Facility," before proceeding to the next site.

9.6.6 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation times and temperatures on Attachments 3 and 5 in the comments section.

9.6.7 Record surface sampling results on Attachments 3 and 5, and file all completed documents in the EM binder.

9.7 Confirm the Sterility of 70% IPA

9.7.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 3 and 5).

9.7.2 Obtain as many contact plates from storage as there are IPA bottles.

9.7.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.7.2.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 3 and 5.

9.7.3 Aseptically remove the contact plate cover. Do not touch the agar surface (If agar is touched, discard the plate and begin again).

9.7.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.7.5 Replace the cover and seal the plate with tape/parafilm.

9.7.6 Label the base of the plate with "IPA" and the IPA lot number/expiration date. Do not record any information on the cover of the plate.

9.7.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation times and temperatures on Attachments 3 and 5.

9.7.8 Record results on Attachments 3 and 5, and file all completed documents in the EM binder.

9.8 Personnel Monitoring

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9.8.1 Refer to the Clean Room Facility Personnel Touch Plate Log (Attachment 6).

9.8.2 Obtain the appropriate quantity of contact plates from storage.

9.8.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.8.2.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachment 6.

9.8.3 Record the compounder's name on Attachment 6.

9.8.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.8.5 Replace the cover and seal the plate with tape/parafilm.

9.8.6 Label the base of the contact plate with the date, the compounder's initials and the hand sampled.

9.8.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation times and temperatures on Attachment 6.

9.8.8 Record personnel monitoring results on Attachment 6, and file all completed documents in the EM binder.

9.9 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

9.10 Alert and Action Limits

9.10.1 Air Sampling (Viable and Non-Viable)

9.10.1.1 Calculate the level of viable airborne particulates as CFU per cubic foot.

9.10.1.2 Calculate the level of non-viable airborne particulates as a quantity of particles ≥0.5μm in diameter per cubic foot.

9.10.1.3 The alert/action limits for air sampling should be derived from historical data. **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 7).**

9.10.2 Surface and Personnel Monitoring

9.10.2.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.10.2.2 The alert/action limits for surface and personnel monitoring should be derived from historical data. **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 7).**

9.11 Investigation and Corrective Actions

9.11.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

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9.11.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized.

9.11.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

- 9.11.3.1 Review of sanitation procedures (repeat if necessary)
- 9.11.3.2 Review of sampling technique
- 9.11.3.3 Review of clean room personnel
- 9.11.3.4 Inspection of sampling media

9.11.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

- 9.11.4.1 Identification of microbial isolates to determine origin
- 9.11.4.2 Review of pressure differential information
- 9.11.4.3 Review of HEPA and clean room certification
- 9.11.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.11.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

10.0 ATTACHMENTS

10.1 Attachment 1 – Receipt of TSA Strips/Contact Plates

10.2 Attachment 2 – Clean Room 1 Air Sampling Log

10.3 Attachment 3 – Clean Room 2 Air Sampling Log

10.4 Attachment 4 – Clean Room 1 Surface Sampling Log

10.5 Attachment 5 – Clean Room 2 Surface Sampling Log

10.4 Attachment 6 – Clean Room Facility Personnel Touch Plate Log

10.5 Attachment 7 – USP Proposed Levels for Air and Surface Monitoring

11.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP.	CR06012
2.0		Updated section 9.3 and attachment 1 to include positive/negative controls. Updated sample identification labels and schematic maps on attachments 2, 3, 4 and 5.	CR06053

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RECEIPT OF TSA STRIPS/CONTACT PLATES

Media Type	Manufacturer	Lot Number	Expiration Date	Received By (Initials/Date)	Incubation Dates of Positive and Negative Controls	Positive Control	Negative Control	Result
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject
☐ Strips					20°C-25°C (room temperature)	☐ Growth	☐ Growth	☐ Accept
☐ Plates					30°C-35°C	☐ No Growth	☐ No Growth	☐ Reject

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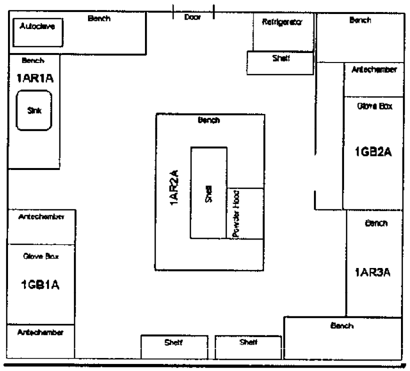
CLEAN ROOM 1 AIR SAMPLING LOG



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Sample	Location	NON-VIABLE AIR SAMPLES		VIABLE AIR SAMPLES		
		Results (Particles/ft^3)	Pass/Fail	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
1GB1A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
1GB2A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
1AR1A	ISO Class 7 Room		☐P ☐F			☐P ☐F
1AR2A	ISO Class 7 Room		☐P ☐F			☐P ☐F
1AR3A	ISO Class 7 Room		☐P ☐F			☐P ☐F

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Non-Viable Air Sampler

Mfg./Model: ______________________

Serial #: ______________________ Calibration Due: ____________

Viable Air Sampler

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Mfg./Model: ______________________

Serial #: ______________________ Calibration Due: ____________

Media Lot #/Expiration Date: ______________________

Comments:

____

____

Performed By: ______________________ **Date:** ____________

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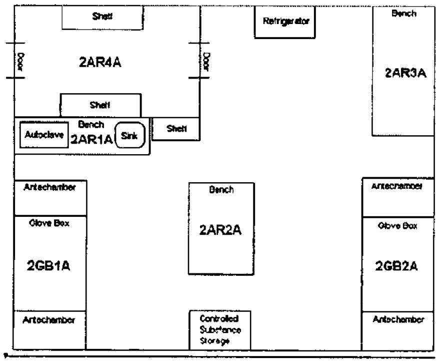
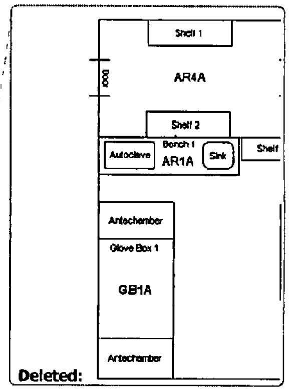
CLEAN ROOM 2 AIR SAMPLING LOG





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Sample	Location	NON-VIABLE AIR SAMPLES		VIABLE AIR SAMPLES		
		Results (Particles/ft^3)	Pass/Fail	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
2GB1A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
2GB2A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
2AR1A	ISO Class 7 Room		☐P ☐F			☐P ☐F
2AR2A	ISO Class 7 Room		☐P ☐F			☐P ☐F
2AR3A	ISO Class 7 Room		☐P ☐F			☐P ☐F
2AR4A	ISO Class 8 Room		☐P ☐F			☐P ☐F

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Non-Viable Air Sampler

Mfg./Model: ______________________

Serial #: ______________________ Calibration Due: ____________

Viable Air Sampler

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Mfg./Model: ______________________

Serial #: ______________________ Calibration Due: ____________

Media Lot #/Expiration Date: ______________________

Comments:

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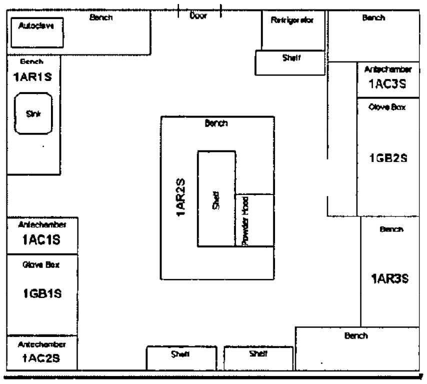
CLEAN ROOM 1 SURFACE SAMPLING LOG



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Sample	Location	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
1GB1S	ISO Class 5 Glove Box			☐P ☐F
1GB2S	ISO Class 5 Glove Box			☐P ☐F
1AC1S	ISO Class 7 Antechamber			☐P ☐F
1AC2S	ISO Class 7 Antechamber			☐P ☐F
1AC3S	ISO Class 7 Antechamber			☐P ☐F
1AR1S	ISO Class 7 Room			☐P ☐F
1AR2S	ISO Class 7 Room			☐P ☐F
1AR3S	ISO Class 7 Room			☐P ☐F
1IPA	Sterile 70% IPA			☐P ☐F

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Media Lot #/Expiration Date: ______________________________

Comments:

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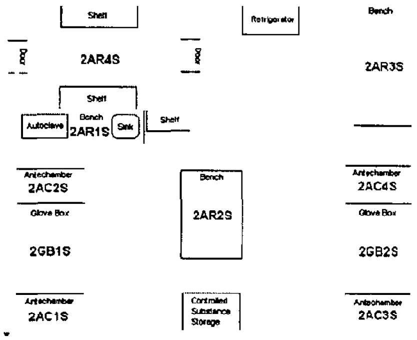
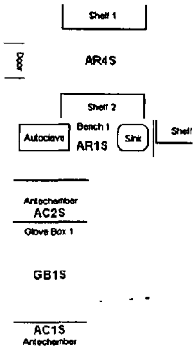
New England Compounding Center

SOP 3.030 Version 2.0

Attachment 4

CLEAN ROOM 2 SURFACE SAMPLING LOG





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Sample	Location	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
2GB1S	ISO Class 5 Glove Box			☐P ☐F
2GB2S	ISO Class 5 Glove Box			☐P ☐F
2AC1S	ISO Class 7 Antechamber			☐P ☐F
2AC2S	ISO Class 7 Antechamber			☐P ☐F
2AC3S	ISO Class 7 Antechamber			☐P ☐F
2AC4S	ISO Class 7 Antechamber			☐P ☐F
2AR1S	ISO Class 7 Room			☐P ☐F
2AR2S	ISO Class 7 Room			☐P ☐F
2AR3S	ISO Class 7 Room			☐P ☐F
2AR4S	ISO Class 8 Room (Shelf)			☐P ☐F
2IPA	Sterile 70% IPA			☐P ☐F

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Media Lot #/Expiration Date:

Comments:

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Reviewed By: ______________________ **Date:** __________

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATE LOG

Media Lot # and Expiration Date	Compounder	Incubation Start Date	Incubation End Date	Results (CFU)	Pass/Fail
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
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table needs to include columns for room temp incubation and actual incubator start and end dates.

OJ 03-29-06

Reviewed By: ______________________ **Date:** __________

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USP PROPOSED LEVELS FOR AIR AND SURFACE MONITORING

Note: Alert/Action Levels are to be determined after historical data is collected.

Levels for Air Sampling

Classifications	Non-Viable Particles (≥0.5µm/ft^3)	Viable Particles (CFU/ft^3)	Alert Level	Action Level
Critical Areas Class 100 (ISO Class 5)	100	< 0.1	N/A	N/A
Non-Critical Areas Class 1,000 – 10,000 (ISO Class 6 – 7)	1,000 – 10,000	< 0.5	N/A	N/A
Support Areas Class 100,000 (ISO Class 8)	100,000	< 2.5	N/A	N/A

Levels for Surface Sampling

Classifications	Surface Monitoring (CFU/contact plate)*	Personnel Monitoring (CFU/contact plate)*	Alert Level	Action Level
Critical Areas Class 100 (ISO Class 5)	3	3 – gloves (5 – mask/gloves)	N/A	N/A
Non-Critical Areas Class 1,000 – 10,000 (ISO Class 6 – 7)	5 (10 including floor)	5 – gloves (10 – mask/gloves)	N/A	N/A
Support Areas Class 100,000 (ISO Class 8)	20 (30 including floor)	15 – gloves (30 – mask/gloves)	N/A	N/A

(*Contact plate areas vary from 24 to 30 square centimeters. When swabbing is used in sampling, the area covered should be greater than or equal to 24cm^2 but no larger than 30cm^2.)

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SOP CHANGE REQUEST

(Page 1 of 2)

Check one: ☑ New ☐ Change **Change Request Log Number:** CR06012

SOP Number/Title: 3.030, Environmental Monitoring of the Clean Room Facility

Version of SOP being changed: N/A **New Version:** 1.0

Description/Text of Change: (see attached Changed Document)
New SOP

Reason for Change Request:
New SOP

Supporting Documentation: (mark one)

☑ None Required ☐ Attached → reference (specify): ____________

Requested Implementation Date: (mark one)

☑ Less than 30 Days ☐ By Date: ____________

Annual SOP Review Requirements: (mark one)

N/A

☐ Complete review was performed to satisfy the requirements of SOP review (see page 2).

☐ Review limited to changes only, SOP review will need to be performed when scheduled.

Check Training Requirements: (mark one)

☑ Read and Understand Memo ☐ Training Session Required

Training Checklist:

☑ No Checklist is Required **OR** TC#__________ has been reviewed and:

☐ No Changes are Required

☐ Checklist needs to be Written/Changes are Required → TC change # ____________

Change Originator:	Anne Avezzano		03-07-06
	Printed Name	Signature	Date
Quality Control:	Barry J. Cadden		03-08-06
	Printed Name	Signature	Date

ORIGINAL
AA 03-07-06

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY	
SOP NUMBER: 3.030	**VERSION NUMBER: 1.0**
Authorized By:	Date: 03-07-06 Dept: LAB
Written By: Anne Avezzano	Date: 02-14-06
Reviewed By:	Date: 03-08-06
Date Effective: 03-08-06	

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for non-viable and viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> “Pharmaceutical Compounding – Sterile Preparations”

4.2 USP Current Version <1116> “Microbiological Evaluation of Clean Rooms and Other Controlled Environments”

4.3 ISO 14644-4 “Clean Rooms and Associated Controlled Environments, Part 4”

4.4 SOP 3.010 “Sterile Compounding Area Requirements”

4.5 SOP 3.020 “Cleaning and Maintenance of the Clean Room Facility”

4.6 SOP 9.090 “Required Garb for Clean Room Facility Access”

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Non-Viable Air Sampler – Device used to provide quantitative analysis of all airborne particles $\geq 0.5 \mu m$ in diameter

5.3 Viable Air Sampler – Device used to provide quantitative analysis of viable airborne viable

5.4 Surface Contact Plate – Device of known surface area providing a convex surface to remove viable particles from a flat work surface

5.5 ISO Classifications

- 5.5.1 ISO Class 5 is equivalent to Class 100.
- 5.5.2 ISO Class 6 is equivalent to Class 1,000.
- 5.5.3 ISO Class 7 is equivalent to Class 10,000.
- 5.5.4 ISO Class 8 is equivalent to Class 100,000.

ORIGINAL
AA 03-07-06

5.6 Alert Level – Signals a potential drift from normal operating conditions when normal levels of viable/non-viable particulate in a controlled environment are exceeded; reaching alert level does not require investigation

5.7 Action Level – Signals a potential drift from normal operating conditions when normal levels of viable/non-viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled once per person daily upon completion of sterile compounding and **prior to cleaning**.

6.2 Surface sampling in the Class 100 (ISO Class 5) area shall be performed weekly upon completion of sterile compounding and **prior to cleaning.**

6.3 Sterility of 70% isopropyl alcohol (IPA) will be confirmed weekly.

6.4 Viable and non-viable air sampling shall be performed at least every six months.

6.5 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 TSA strips for viable air samplers (if applicable)

7.4 Viable air samplers with sterilized impeller and shroud (BioTest RCS or equivalent)

7.5 Non-viable air sampler (Met One or equivalent)

7.6 Appropriate user manuals

7.7 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from “clean” areas to “dirty” areas.

9.0 PROCEDURE

9.1 Upon receipt of commercially prepared TSA contact plates or TSA strips, retain the manufacturer's certificate of testing and conformance.

9.2 Verify that the certificate of conformance documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

  9.2.1 Document receipt of the media on the Receipt of TSA Strips/Contact Plates form (Attachment 1) and place the form along with the manufacturer's certificates in a designated binder.

  9.2.2 Store the media according to the manufacturer's recommendation (usually 2°C-8°C) in a monitored refrigerator.

9.3 Non-Viable Air Sampling

  9.3.1 Refer to the appropriate Clean Room Facility Air Sampling Log (Attachments 2 and 4).

ORIGINAL
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9.3.2 Verify the air sampler is within calibration and document the manufacturer/model, serial number, and calibration due date on Attachments 2 and 4.

9.3.3 Sanitize the air sampler exterior prior to entry into the clean room facility.

9.3.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.3.5 Prepare the air sampler according to the manufacturer's instructions. The volume of air sampled in all areas will be one cubic foot.

9.3.6 Place the air sampler in the desired location and turn on. **Do not stand over the sampler while in operation.**

9.3.7 Perform non-viable air sampling beginning in the Class 100 (ISO Class 5) glove box, followed by the Class 10,000 (ISO Class 7) antechamber, then the Class 10,000 (ISO Class 7) buffer/ preparation room and concluding in the Class 100,000 (ISO Class 8) room.

9.3.8 Record non-viable air sampling results on Attachments 2 and 4, and file all completed documents in the EM binder.

9.4 Viable Air Sampling

9.4.1 Refer to the appropriate Clean Room Facility Air Sampling Log (Attachments 2 and 4).

9.4.2 Obtain the appropriate quantity of media from storage.

9.4.2.1 Inspect each strip/plate and discard any damaged or contaminated media and replace.

9.4.2.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 2 and 4.

9.4.3 Verify the air sampler is within calibration and document the manufacturer/model, serial number and calibration due date on Attachments 2 and 4.

9.4.4 Sanitize the air sampler exterior prior to entry into the clean room facility.

9.4.5 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.4.6 Set up the air sampler according to the manufacturer's instructions.

9.4.7 The volume of air sampled in the Class 100 (ISO Class 5) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

9.4.8 Perform viable air sampling beginning in the Class 100 (ISO Class 5) glove box, followed by the Class 10,000 (ISO Class 7) antechamber, then the Class 10,000 (ISO Class 7) buffer/ preparation room and concluding in the Class 100,000 (ISO Class 8) room.

9.4.8.1 Aseptically remove an agar strip/contact plate from its wrapper. Do not touch the agar surface (If agar is touched, discard the strip/contact plate and begin again).

9.4.8.2 If using agar strips, slide the strip into the rotor at the guide plate with the agar surface facing inward until the strip closes the drum slot. If using

ORIGINAL
AA 03-07-06

contact plates aseptically remove the cap from the sampler and secure the plate between the metal prongs.

9.4.8.3 Place the air sampler in the desired location and turn on. **Do not stand over the sampler while in operation.**

9.4.8.4 The air sampler will automatically turn off at the conclusion of the sampling period.

9.4.8.5 Aseptically remove the strip/contact plate from the sampler. Place the agar strip in its protective cover, or replace the lid of the contact plate.

9.4.8.6 Seal the strip/contact plate with a slide seal or tape/parafilm.

9.4.8.7 Label the strip with the sample location and document on Attachments 2 and 4.

9.4.9 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation time and temperatures on Attachments 2 and 4 in comments section.

9.4.10 Record viable air sampling results on Attachments 2 and 4, and file all completed documents in the EM binder.

9.5 Surface Sampling

9.5.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 3 and 5).

9.5.2 Surface samples of the Class 100 (ISO Class 5) area shall be taken weekly upon completion of sterile compounding and **prior to cleaning.**

9.5.3 Obtain the appropriate quantity of contact plates from storage.

9.5.3.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.5.3.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 3 and 5.

9.5.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.5.5 Sampling technique:

9.5.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Do not touch the agar surface (If agar is touched, discard the plate and begin again).

9.5.5.2 Gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface.

9.5.5.3 Replace the cover and seal the plate with tape/parafilm.

9.5.5.4 Record the site location on the base of the plate. Do not record any information on the cover of the plate.

9.5.5.5 Clean the sample site per SOP 3.020, "Cleaning and Maintenance of the Clean Room Facility," before proceeding to the next site.

ORIGINAL
AA 03-07-06

9.5.6 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation times and temperatures on Attachments 3 and 5 in the comments section.

9.5.7 Record surface sampling results on Attachments 3 and 5, and file all completed documents in the EM binder.

9.6 Confirm the Sterility of 70% IPA

9.6.1 Refer to the appropriate Clean Room Facility Surface Sampling Log (Attachments 3 and 5).

9.6.2 Obtain as many contact plates from storage as there are IPA bottles.

9.6.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.6.2.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachments 3 and 5.

9.6.3 Aseptically remove the contact plate cover. Do not touch the agar surface (If agar is touched, discard the plate and begin again).

9.6.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.6.5 Replace the cover and seal the plate with tape/parafilm.

9.6.6 Label the base of the plate with "IPA" and the IPA lot number/expiration date. Do not record any information on the cover of the plate.

9.6.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation times and temperatures on Attachments 3 and 5.

9.6.8 Record results on Attachments 3 and 5, and file all completed documents in the EM binder.

9.7 Personnel Monitoring

9.7.1 Refer to the Clean Room Facility Personnel Touch Plate Log (Attachment 6).

9.7.2 Obtain the appropriate quantity of contact plates from storage.

9.7.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.7.2.2 Verify media is within expiration dating, and record media lot number and expiration date on Attachment 6.

9.7.3 Record the compounder's name on Attachment 6.

9.7.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.7.5 Replace the cover and seal the plate with tape/parafilm.

9.7.6 Label the base of the contact plate with the date, the compounder's initials and the hand sampled.

ORIGINAL
AA 03-07-06

9.7.7 Incubate all exposed samples for 72-84 hours at 20°C-25°C or room temperature, and then incubate for an additional 48-72 hours at 30°C-35°C. (Samples may be shipped to a contract lab for incubation and analysis.) Document incubation times and temperatures on Attachment 6.

9.7.8 Record personnel monitoring results on Attachment 6, and file all completed documents in the EM binder.

9.8 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

9.9 Alert and Action Limits

9.9.1 Air Sampling (Viable and Non-Viable)

9.9.1.1 Calculate the level of viable airborne particulates as CFU per cubic foot.

9.9.1.2 Calculate the level of non-viable airborne particulates as a quantity of particles ≥0.5μm in diameter per cubic foot.

9.9.1.3 The alert/action limits for air sampling should be derived from historical data. **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 7).**

9.9.2 Surface and Personnel Monitoring

9.9.2.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.9.2.2 The alert/action limits for surface and personnel monitoring should be derived from historical data. **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 7).**

9.10 Investigation and Corrective Actions

9.10.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

9.10.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized.

9.10.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.3.1 Review of sanitation procedures (repeat if necessary)

9.10.3.2 Review of sampling technique

9.10.3.3 Review of clean room personnel

9.10.3.4 Inspection of sampling media

9.10.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.4.1 Identification of microbial isolates to determine origin

ORIGINAL
AA 03-07-06

9.10.4.2 Review of pressure differential information

9.10.4.3 Review of HEPA and clean room certification

9.10.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.10.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

10.0 ATTACHMENTS

10.1 Attachment 1 – Receipt of TSA Strips/Contact Plates

10.2 Attachment 2 – Clean Room 1 Air Sampling Log

10.3 Attachment 3 – Clean Room 2 Air Sampling Log

10.4 Attachment 4 – Clean Room 1 Surface Sampling Log

10.5 Attachment 5 – Clean Room 2 Surface Sampling Log

10.4 Attachment 6 – Clean Room Facility Personnel Touch Plate Log

10.5 Attachment 7 – USP Proposed Levels for Air and Surface Monitoring

11.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP.	CR06012

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RECEIPT OF TSA STRIPS/CONTACT PLATES

Media Type	Manufacturer	Lot Number	Expiration Date	Received By (Initials/Date)
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				
☐ Strips ☐Contact Plates				

Reviewed By: ______________________________ **Date:** ______________

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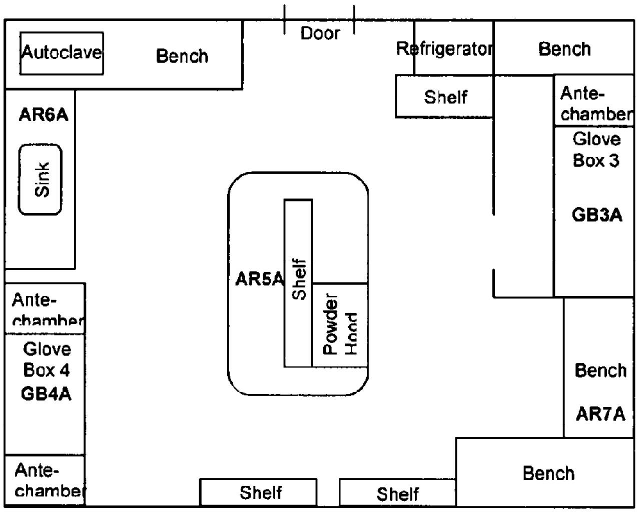
AA 03-07-06

CLEAN ROOM 1 AIR SAMPLING LOG



Sample	Location	NON-VIABLE AIR SAMPLES		VIABLE AIR SAMPLES		
		Results (Particles/ft^3)	Pass/Fail	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
GB3A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
GB4A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
AR5A	ISO Class 7 Room		☐P ☐F			☐P ☐F
AR6A	ISO Class 7 Room		☐P ☐F			☐P ☐F
AR7A	ISO Class 7 Room		☐P ☐F			☐P ☐F

Non-Viable Air Sampler

Mfg./Model: ______________________________

Serial #: ______________________________ Calibration Due: ______________

Viable Air Sampler

Mfg./Model: ______________________________

Serial #: ______________________________ Calibration Due: ______________

Media Lot #/Expiration Date: ______________________________

Comments:

____

____

Performed By: ______________________________ **Date:** ______________

Reviewed By: ______________________________ **Date:** ______________

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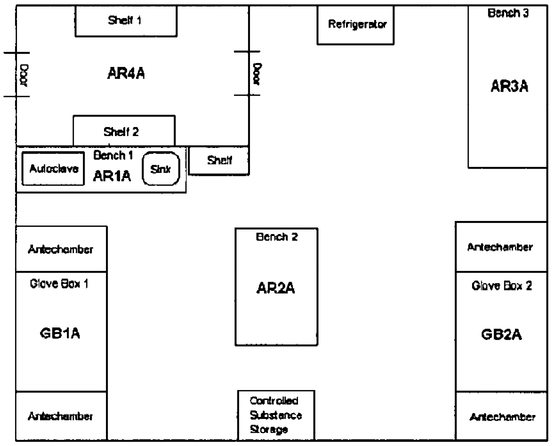
AA 03-07-06

CLEAN ROOM 2 AIR SAMPLING LOG



Sample	Location	NON-VIABLE AIR SAMPLES		VIABLE AIR SAMPLES		
		Results (Particles/ft^3)	Pass/Fail	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
GB1A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
GB2A	ISO Class 5 Glove Box		☐P ☐F			☐P ☐F
AR1A	ISO Class 7 Room		☐P ☐F			☐P ☐F
AR2A	ISO Class 7 Room		☐P ☐F			☐P ☐F
AR3A	ISO Class 7 Room		☐P ☐F			☐P ☐F
AR4A	ISO Class 8 Room		☐P ☐F			☐P ☐F

Non-Viable Air Sampler

Mfg./Model: ______________________________

Serial #: ______________________________ Calibration Due: ______________

Viable Air Sampler

Mfg./Model: ______________________________

Serial #: ______________________________ Calibration Due: ______________

Media Lot #/Expiration Date: ____

Comments:

____

____

Performed By: ____________________________________ **Date:** ____________

Reviewed By: ____________________________________ **Date:** ____________

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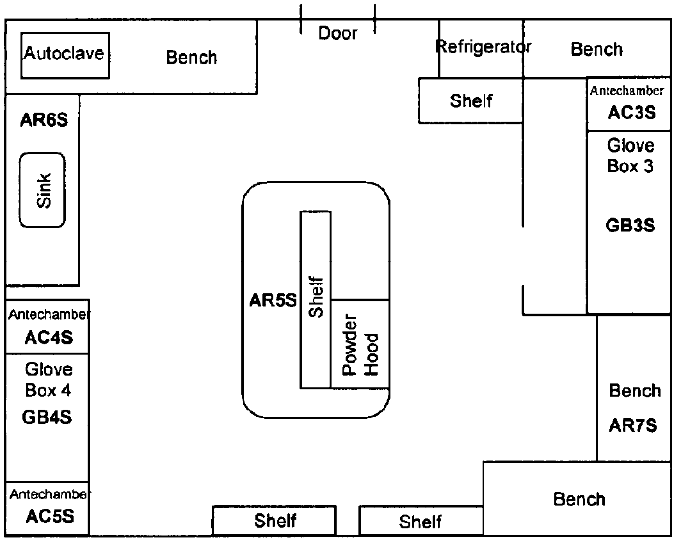
CLEAN ROOM 1 SURFACE SAMPLING LOG



Sample	Location	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
GB3S	ISO Class 5 Glove Box			☐P ☐F
GB4S	ISO Class 5 Glove Box			☐P ☐F
AC3S	ISO Class 7 Antechamber			☐P ☐F
AC4S	ISO Class 7 Antechamber			☐P ☐F
AC5S	ISO Class 7 Antechamber			☐P ☐F
AR5S	ISO Class 7 Room			☐P ☐F
AR6S	ISO Class 7 Room			☐P ☐F
AR7S	ISO Class 7 Room			☐P ☐F
IPA	Sterile 70% IPA			☐P ☐F

Media Lot #/Expiration Date: ______________________________

Comments:

____

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Performed By: ______________________________ **Date:** ______________

Reviewed By: ______________________________ **Date:** ______________

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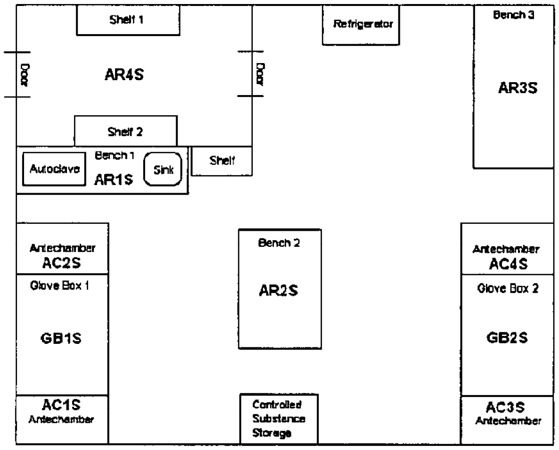
AA-03-07-06

CLEAN ROOM 2 SURFACE SAMPLING LOG



Sample	Location	Incubation Dates (If Applicable)	Results (CFU)	Pass/Fail
GB1S	ISO Class 5 Glove Box			☐P ☐F
GB2S	ISO Class 5 Glove Box			☐P ☐F
AC1S	ISO Class 7 Antechamber			☐P ☐F
AC2S	ISO Class 7 Antechamber			☐P ☐F
AC3S	ISO Class 7 Antechamber			☐P ☐F
AC4S	ISO Class 7 Antechamber			☐P ☐F
AR1S	ISO Class 7 Room			☐P ☐F
AR2S	ISO Class 7 Room			☐P ☐F
AR3S	ISO Class 7 Room			☐P ☐F
AR4S	ISO Class 8 Room (Shelf)			☐P ☐F
IPA	Sterile 70% IPA			☐P ☐F

Media Lot #/Expiration Date: ______________________

Comments:

____

____

Performed By: ______________________ **Date:** __________

Reviewed By: ______________________ **Date:** __________

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AA 03-07-06

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATE LOG

Media Lot # and Expiration Date	Compounder	Incubation Start Date	Incubation End Date	Results (CFU)	Pass/Fail
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F
					☐P ☐F

Reviewed By: ______________________ **Date:** ____________

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AA 03-07-06

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 **VERSION NUMBER: 4.0**

Sterile Laboratory
Effective Date 09-22-08

Originator:
Reviewer:

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for viable and non-viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644-4 "Clean Rooms and Associated Controlled Environments", Part 4

4.4 SOP 3.010 "Sterile Compounding Area Requirements"

4.5 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.6 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Viable Particle - A viable particle is a particle that contains one or more living microorganisms.

5.3 Viable Air Sampler - Device used to sample microorganisms in the air.

5.4 Non-Viable Air Sampling - Total particle count. Includes viable particles but does not test for presence of microorganisms.

5.5 Surface Contact Plate - Agar plate used to sample surfaces for microorganisms by direct application. The agar contains neutralizers to inactivate residual disinfectants.

5.6 ISO Classifications

- 5.6.1 ISO Class 4 is equivalent to Class 10 (glove box, antechamber).
- 5.6.2 ISO Class 6 is equivalent to Class 1,000 (main clean room).
- 5.6.3 ISO Class 7 is equivalent to Class 10,000 (gown/crimp room).
- 4.1.1 ISO Class 8 is equivalent to Class 100,000 (prep room).

ORIGINAL
09-22-08

5.7 Alert Level -Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching alert level does not require investigation. (Attachment 8)

5.8 Action Level - Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action. (Attachment 8)

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled upon completion of sterile compounding and **prior to cleaning**.

6.2 Surface sampling in the glove boxes and antechambers Class 10(ISO Class 4), Class 1000 main clean room(ISO Class 6), Class10,000(ISO Class 7) gown/crimp room, Class100,000(ISO Class 8)prep room, area shall be performed weekly, **prior to cleaning**.

6.3 Sterility of 70% isopropyl alcohol (IPA) will be confirmed weekly.

6.4 Viable air sampling shall be performed weekly.

6.5 Non-Viable air sampling shall be performed at least every six months.

6.6 The Pharmacist-in-charge or the Quality Control officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 Viable air sampler with sterilized impeller and shroud (Model # SAS180)

7.4 Appropriate user manuals

7.5 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from "clean" areas to "dirty" areas.

9.0 PROCEDURE

9.1 Upon receipt of commercially prepared TSA contact plates, retain the manufacturer's Certificate of Analysis (CofA). Document receipt of the media on Receipt of Contact plates (Attachment 1).

9.2 Verify that the (CofA) documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

9.2.1 Remove two plates from new lot of media received for positive and negative controls.

9.2.2 Label one plate "Positive" and the other plate "Negative," and write the date on each plate.

9.2.3 Do not expose the agar surface of the "Negative" plate. Seal the contact plate with parafilm.

9.2.4 For the "Positive" control expose the agar to air for 15 minutes. Seal the contact plate with parafilm.

9.2.5 Incubate for 5 days at 30°C-35°C. Document on Attachment 1.

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9.2.6 If the positive control has no growth or the negative control has growth, the lot must be rejected.

9.2.7 Place the completed Attachment 1, along with the (CofA) in a designated binder.

9.2.8 Store all acceptable media according to the manufacturer's recommendation in a monitored refrigerator. (2°C - 8°C).

9.3 Viable Air Sampling

9.3.1 Set up the air sampler according to the manufacturer's instructions.

9.3.2 Sanitize the exterior of the air sampler prior to use with a low-lint wipe, saturated with sterile 70% IPA.

9.3.3 If the sampler is being moved from a dirty to clean location during sampling, repeat exterior sanitization.

9.3.4 Make sure the air sampler is programmed with the following parameters:

Sample Time	**Air Volume/Minute**	**Total Air Volume**
5.5 Minutes	180 Liters	1000 liters (35ft^3)

9.3.5 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.3.6 Document all data on the appropriate Attachments.

9.3.7 Obtain the appropriate quantity of media from storage.

9.3.7.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.3.7.2 Verify media is within expiration date and record media lot number and expiration date on Attachment 6.

9.3.7.3 Aseptically remove an agar contact plate from its package. Make sure that the contact plate covers remains on.

9.3.7.4 Aseptically remove the outer protective cap from the sampler and unscrew the aspirating head.

9.3.7.5 Secure the plate between the metal prongs. Once secure, remove the contact plate cover and immediately replace the aspirating head and screw on tightly.

NOTE: *Do not touch the agar surface (If agar is touched, discard the contact plate).*

9.3.8 Place the air sampler in the desired location at cart or bench top height. Orient the air sampler in a vertical position facing the ceiling and turn on.
Do not place arms over sampler while in operation.

9.3.8.1 The air sampler will automatically turn off at the conclusion of the sampling period.

9.3.8.2 Aseptically remove the contact plate from the sampler. Replace the lid of the contact plate.

9.3.8.2.1 Inspect the contact plate to ensure the impingement marks are present.

9.3.8.2.2 If impingement marks are not present, the sample is invalid and shall be repeated with a new contact plate.

9.3.8.3 Seal the contact plate with parafilm.

ORIGINAL
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9.3.8.4 Record the site location on the base of the plate, initial and date. Do not record any information on the cover plate.

9.3.8.5 Invert the samples and incubate for as follows.

9.3.8.6 5 days at 30-35 °C.

NOTE: If 5th day of incubation falls on a non-business day, then the plates shall be incubated at that temperature for the remainder of the 7 days. Do not exceed 7 days of incubation.

NOTE: Samples may be shipped to a contract lab for incubation and analysis.

9.4 Non-Viable Air Sampling

9.4.1 Non-viable air sampling shall be performed every 6 months along with Room/Hood Certification.

9.4.2 Sampling shall be performed by an approved vendor using calibrated equipment.

9.4.3 File all completed documents in the designated binder.

9.5 Surface Sampling

9.5.1 Document all data on the appropriate Attachments.

9.5.2 Surface sampling in the glove boxes and antechambers - Class 10 (ISO 4), Class 1000 (ISO 6)main clean room, Class 10,000 (ISO 7)gown/crimp room, Class 100,000 (ISO 8) prep room area shall be performed weekly, **prior to cleaning**

9.5.3 Obtain the appropriate quantity of contact plates from storage.

9.5.3.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.5.3.2 Verify media is within expiration date and record media lot number and expiration date on appropriate Attachment.

9.5.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.5.5 Sampling technique:

9.5.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface for 10 seconds.

9.5.5.2 Replace the cover and seal the plate with parafilm.

9.5.5.3 Record the site location on the base of the plate. Do not record any information on the cover of the plate.

9.5.5.4 Clean the sample site with sterile 70% IPA before proceeding to the next site.

9.5.6 Incubate for 5 days 30°C-35°C.

9.5.7 Record surface sampling results on Attachment 2, and file all completed documents in the EM binder.

9.6 Confirm the Sterility of 70% IPA

9.6.1 Refer to the appropriate Attachment for Surface Sampling Log

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9.6.2 Obtain two contact plates from storage and test two random sterile 70% IPA bottles.

  9.6.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

  9.6.2.2 Verify media is within expiration date, and record media lot number and expiration date on Attachment 2.

9.6.3 Aseptically remove the contact plate cover.

NOTE: *Do not touch the agar surface (If agar is touched, discard the contact plate).*

9.6.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.6.5 Replace the cover and seal the plate with parafilm.

9.6.6 Label the base of the plate with "IPA" and the IPA lot number/expiration date. Do not record any information on the cover of the plate.

9.6.7 Incubate for 5 days at 30°C-35°C.

9.6.8 Record results on Attachment 2, and file all completed documents in the EM binder.

9.7 Personnel Monitoring

9.7.1 Refer to the Clean Room Facility Personnel Touch Plate Log (Attachment 7).

9.7.2 Obtain the appropriate quantity of contact plates from storage.

  9.7.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

  9.7.2.2 Verify media is within expiration date.

  9.7.2.3 Label the base of the contact plate with the date, the pharmacist/technician initials, the hand sampled and what product is being compounded.

  9.7.2.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.7.3 Replace the cover and seal the plate with parafilm.

9.7.4 Incubate for 5 days at 30°C-35°C.

9.7.5 Record personnel monitoring results on Attachment 7 and file all completed documents in the EM binder.

9.8 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

9.9 Alert and Action Limits

9.9.1 Air Sampling (Viable)

9.9.2 Calculate the level of viable airborne particulates as CFU per cubic foot. The volume of air sampled in the Class 10 (ISO 4) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

  9.9.2.1 The alert/action limits for air sampling should be derived from historical data. * **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 8).**

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9.9.3 Surface and Personnel Monitoring

9.9.3.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.9.3.2 The alert/action limits for surface and personnel monitoring should be derived from historical data. * **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 8).**

9.10 Investigation and Corrective Actions

9.10.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

9.10.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized.

9.10.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.3.1 Review of sanitation procedures

9.10.3.2 Review of sampling technique

9.10.3.3 Review of clean room personnel

9.10.3.4 Inspection of sampling media

9.10.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.4.1 Identification of microbial isolates to determine origin

9.10.4.2 Review of pressure differential information

9.10.4.3 Review of HEPA and clean room certification

9.10.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.10.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

9.11 Non-Routine Samples

9.11.1 Non-routine samples that are not listed on the Viable and Surface Sampling Forms may be taken at a desired location.

9.11.2 Take the sample according to the appropriate air or surface sampling procedure above.

9.11.3 Document air/surface sample location and results on Attachment 4.

9.11.4 Non-routine samples are investigational and shall not be compared to alert/action values. Do not generate an alert or action as described in 9.10 for non-routine samples.

9.12 Reporting Results

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9.12.1 Remove samples from the incubator. Record stop times on the appropriate attachment.

9.12.2 Count all colonies on the plate and document results for each category below.

- Bacteria
- Mold (Count or indicate presence)
- Total Counts of Bacteria and Mold combined

10.0 ATTACHMENTS

10.1 Attachment 1 - Receipt of Contact Plates
10.2 Attachment 2 - Clean Room Surface Sampling
10.3 Attachment 3 - Clean Room Surface Sampling Diagram
10.4 Attachment 4 - Random Air/Surface Sample Form
10.5 Attachment 5 - Clean Room Viable Air Sampling Diagram
10.6 Attachment 6 - Clean Room Viable Air Sampling
10.7 Attachment 7 - Clean Room Facility Personnel Touch Plate Log
10.8 Attachment 8 - Levels for Air and Surface Monitoring

1.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06012
2.0	04/06/06	Updated section 9.3 and attachment 1 to include positive/negative controls. Updated sample identification labels and schematic maps on attachments 2, 3, 4 and 5.	CR06053
3.0	11/30/07	Taking out TSA Strips, non-viable samples, fixing iso/ classes not correct	CR07018
4.0	09-22-08	Re did attachments for new clean room, Minor changes	CR08017

ORIGINAL
smk
0922-08

RECEIPT OF CONTACT PLATES - ATTACHMENT 1

Quantity Rec'd (i.e. boxes of 50 plates)	*Manufacturer*	*Lot Number*	*Expiration Date*	*Received By (Initials/Date)*	*Incubation Dates of Positive and Negative Controls 30°C-35°C*	*Positive Control*	*Negative Control*	*Results (CFU)*
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject

Quality Control: **Date:**
Revi wed By: **Date:**

ORIGINAL
BWK 04-22-08

CLEAN ROOM SURFACE SAMPLING - ATTACHMENT 2
(Page 2 of 2)

Sample Location	Description	Results			Alert/ Action
		Bacteria CFU	*Mold CFU*	*Total CFU*	
SinkS	Sink in Crimp Room				☐Al ☐Ac
CrimpS	Crimping Bench				☐Al ☐Ac
1RBS	Random Bin				☐Al ☐Ac
2RBS	Random Bin				☐Al ☐Ac
1GRFS	Gown Room -- Near Hall				☐Al ☐Ac
2GRFS	Gown Room – Near Clean room				☐Al ☐Ac
1PFS	Prep Room – Near Incubator				☐Al ☐Ac
2PFS	Prep Room – Near Warehouse				☐Al ☐Ac
1FLRS	Clean Room Floor				☐Al ☐Ac
2FLRS	Clean Room Floor				☐Al ☐Ac
3FLRS	Clean Room Floor				☐Al ☐Ac
4FLRS	Clean Room Floor				☐Al ☐Ac
5FLRS	Clean Room Floor				☐Al ☐Ac
6FLRS	Clean Room Floor				☐Al ☐Ac
1IPAS	Isopropyl Alcohol				☐Al ☐Ac
2IPAS	Isopropyl Alcohol				☐Al ☐Ac

Alert	**Action**
1 CFU ISO 4 (class 10) Glove box, Antechambers	2+ CFU
3 CFU ISO 6 (class 1,000) Main Clean room	5+ CFU
5 CFU ISO 7 (class 10,000) Gown room, Crimp room	7+ CFU
8 CFU ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling: Media Lot: Exp Date:

Quality Control: Date:
Reviewed By: Date:

ORIGINAL
04-22-08

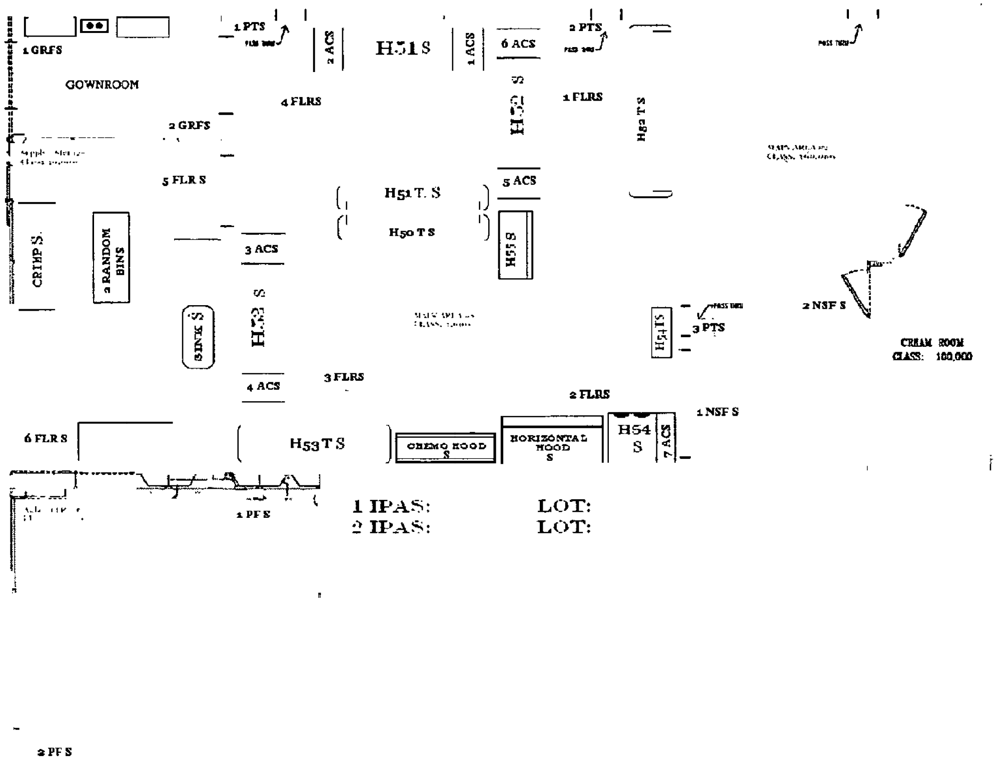
CLEAN ROOM SURFACE SAMPLING - ATTACHMENT 2

(Page 1 of 2)

Sample Location	Description	Results			Alert/ Action
		Bacteria CFU	*Mold CFU*	*Total CFU*	
H51S	Hood 1				☐Al ☐Ac
H52S	Hood 2				☐Al ☐Ac
H53S	Hood 3				☐Al ☐Ac
H54S	Hood 4				☐Al ☐Ac
H55S	Hood 5				☐Al ☐Ac
1ACS	Hood 1 Antechamber (Right Side)				☐Al ☐Ac
2ACS	Hood 1 Antechamber (Left Side)				☐Al ☐Ac
3ACS	Hood 2 Antechamber (Right Side)				☐Al ☐Ac
4ACS	Hood 2 Antechamber (Left Side)				☐Al ☐Ac
5ACS	Hood 3 Antechamber (Left Side)				☐Al ☐Ac
6ACS	Hood 3 Antechamber (Right Side)				☐Al ☐Ac
7ACS	Hood 4 Antechamber				☐Al ☐Ac
ChemoS	Chemo Hood				☐Al ☐Ac
HorizS	Horizontal Hood				☐Al ☐Ac
H50TS	Table 1				☐Al ☐Ac
H51TS	Table 2				☐Al ☐Ac
H52TS	Table 3				☐Al ☐Ac
H53TS	Table 4				☐Al ☐Ac
H54TS	Table 5				☐Al ☐Ac
1PTS	Pass - thru				☐Al ☐Ac
2PTS	Pass - thru				☐Al ☐Ac
3PTS	Pass - thru				☐Al ☐Ac

ORIGINAL
04-22-08

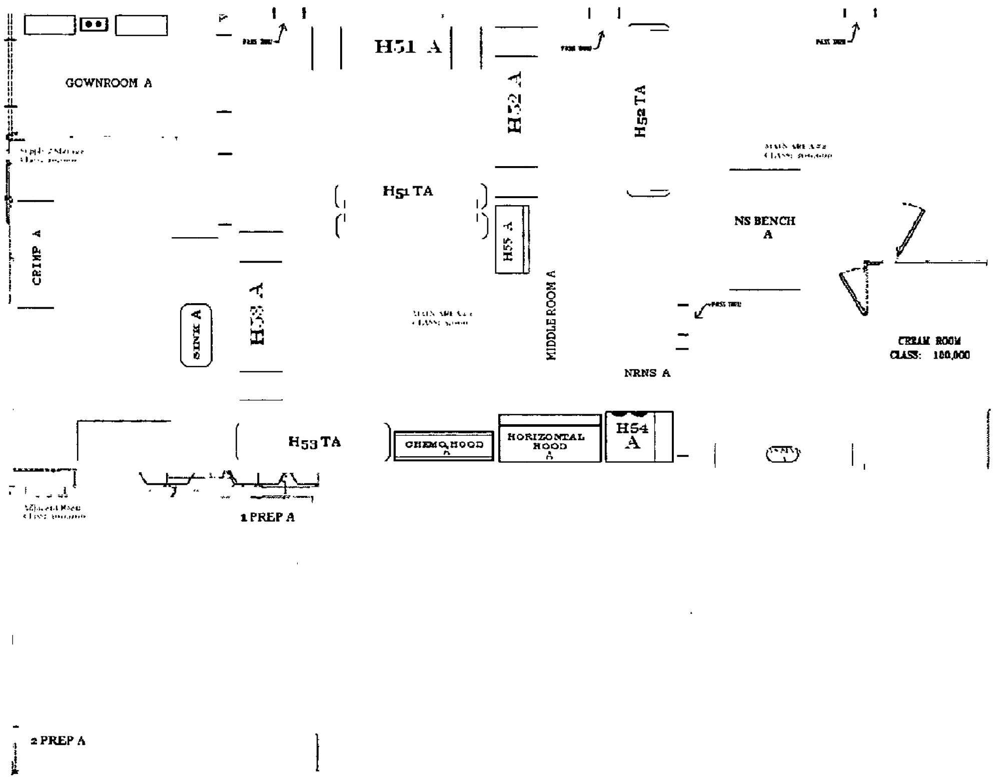
Clean Room Surface Sampling Diagram - Attachment 3



1 IPAS: LOT:
2 IPAS: LOT:

ORIGINAL
AWK
04-22-08

Clean Room Viable Air Sampling Diagram - Attachment 5



ORIGINAL
09-22-05

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 **VERSION NUMBER: 4.0**

CLEAN ROOM VIABLE AIR SAMPLING - ATTACHMENT 6

Page1 of 1

Sample Location	Description	Results			Alert/Action
		Bacteria CFU	*Mold CFU*	*Total CFU*	
H51A	Hood 1				☐Al ☐Ac
H52A	Hood 2				☐Al ☐Ac
H53A	Hood 3				☐Al ☐Ac
H54A	Hood 4				☐Al ☐Ac
H55A	Hood 5				☐Al ☐Ac
ChemoA	Chemo Hood				☐Al ☐Ac
HorizA	Horizontal Hood				☐Al ☐Ac
H51TA	Table 2				☐Al ☐Ac
H52TA	Table 3				☐Al ☐Ac
H53TA	Table 4				☐Al ☐Ac
GownroomA	Gowning Area				☐Al ☐Ac
SinkA	Sink Area				☐Al ☐Ac
CrimpA	Crimping Bench				☐Al ☐Ac
MiddleroomA	Middle of Room				☐Al ☐Ac
NRNSA	Near Non-Sterile Lab				☐Al ☐Ac
1PrepA	Prep Room – Near Incubator				☐Al ☐Ac
2PrepA	Prep Room – Near Warehouse				☐Al ☐Ac

Alert		**Action**
1 CFU	ISO 4 (class 10) Glove box, Antechambers	2+ CFU
2 CFU	ISO 6 (class 1,000) Main Clean room	3+ CFU
5 CFU	ISO 7 (class 10,000) Gown room, Crimp room	8+ CFU
8 CFU	ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling: Media Lot: Exp Date:
Sampler Mfg/Model: Serial #: Calibration Due Date:

Quality Control: Date:
Reviewed By: Date:

AWM 08-22-08

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATE LOG - ATTACHMENT 7

Media Lot # and Exp Date	Rph/Tech	Location and Product Being worked on	Incubation for 5 days at 30°C - 35°C	Results (CFU)	Alert / Action
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac

Alert Level 1+ CFU
Action Level 2+ CFU

Quality Control: Date:

Reviewed By: Date:

ORIGINAL
4/MK
09.2.08

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 **VERSION NUMBER: 4.0**

LEVELS FOR AIR AND SURFACE MONITORING - ATTACHMENT 8

Note: ** Alert/Action Levels are to be determined after historical data is collected**

Levels for Air Sampling

Classifications	Alert Level	Action Level
ISO 4 (Class 10) Glove box, Antechambers	1 CFU	2+ CFU
ISO 6 (Class 1,000) Main Clean Room	2 CFU	3+ CFU
ISO 7(Class 10,000) Gown room, Crimp Room	5 CFU	8+ CFU
ISO Class 8 (Class 100,000) Prep Room	8 CFU	10+ CFU

Levels for Surface Sampling

Classifications			Alert Level	Action Level
ISO 4 (Class 10) Glove box, Antechambers			1 CFU	2+ CFU
ISO 6 (Class 1,000) Main Clean Room			3 CFU	5+ CFU
ISO 7(Class 10,000) Gown room, Crimp Room			5 CFU	7+ CFU
ISO Class 8 (Class 100,000) Prep Room			8 CFU	10+CFU

ORIGINAL

AMK
09-22-08

Clean Room Air Sampling

Attachment 5

		Results			
Sample Location	Description	Bacteria CFU	Mold CFU	Total CFU	Alert/Action
H1	Hood 1				☐ Alert ☐ Action
H2	Hood 2				☐ Alert ☐ Action
H3	Hood 3				☐ Alert ☐ Action
H4	Hood 4				☐ Alert ☐ Action
H5	Hood 5				☐ Alert ☐ Action
CHEMO	Chemo				☐ Alert ☐ Action
HORIZ 1	Horizontal 1				☐ Alert ☐ Action
HORIZ 2A	Horizontal 2A				☐ Alert ☐ Action
HORIZ 2B	Horizontal 2B				☐ Alert ☐ Action
HORIZ 2C	Horizontal 2C				☐ Alert ☐ Action
A1	By entrance & Hood 1				☐ Alert ☐ Action
A2	By hood 3 & Pass thru				☐ Alert ☐ Action
A3	By chemo & horiz 1				☐ Alert ☐ Action
A4	By horiz 2C & hood 5				☐ Alert ☐ Action
CRIMP STATION	Crimp Station				☐ Alert ☐ Action
SINK STATION	Sink Station				☐ Alert ☐ Action
GOWN ROOM	Gown Room				☐ Alert ☐ Action
PREP ROOM	Prep Room				☐ Alert ☐ Action

Quality Control: Date:

Reviewer: Date:

3.030

USP PROPOSED LEVELS FOR AIR AND SURFACE MONITORING

Note: Alert/Action Levels are to be determined after historical data is collected.

Levels for Air Sampling

Classifications	Non-Viable Particles $(\geq 0.5 \mu m/ft^3)$	Viable Particles (CFU/ft^3)	Alert Level	Action Level
Critical Areas Class 100 (ISO Class 5)	100	< 0.1	**N/A**	**N/A**
Non-Critical Areas Class 1,000 – 10,000 (ISO Class 6 – 7)	1,000 – 10,000	< 0.5	**N/A**	**N/A**
Support Areas Class 100,000 (ISO Class 8)	100,000	< 2.5	**N/A**	**N/A**

Levels for Surface Sampling

Classifications	Surface Monitoring (CFU/contact plate)*	Personnel Monitoring (CFU/contact plate)*	Alert Level	Action Level
Critical Areas Class 100 (ISO Class 5)	3	3 – gloves (5 – mask/gloves)	**N/A**	**N/A**
Non-Critical Areas Class 1,000 – 10,000 (ISO Class 6 – 7)	5 (10 including floor)	5 – gloves (10 – mask/gloves)	**N/A**	**N/A**
Support Areas Class 100,000 (ISO Class 8)	20 (30 including floor)	15 – gloves (30 – mask/gloves)	**N/A**	**N/A**

(*Contact plate areas vary from 24 to 30 square centimeters. When swabbing is used in sampling, the area covered should be greater than or equal to $24cm^2$ but no larger than $30cm^2$.)

ORIGINAL
AA 03-07-06

3.030

RANDOM AIR/SURFACE SAMPLING - ATTACHMENT 4

Air/Surface Sample Location	Description	Results		
		Bacteria CFU	***Mold CFU***	***Total CFU***

Date of Sampling:
Media Lot#:
Exp Date:
Sampler Mfg/Model:
Calibration Due Date:

Quality Control:
Date:

Reviewed By:
Date:

ORIGINAL

09-22-08

CLEAN ROOM VIABLE AIR SAMPLING - ATTACHMENT 6

Page 1 of 1

Sample Location	Description	Results			Alert/Action
		Bacteria CFU	*Mold CFU*	*Total CFU*	
H51A	Hood 1				☐Al ☐Ac
H52A	Hood 2				☐Al ☐Ac
H53A	Hood 3				☐Al ☐Ac
H54A	Hood 4				☐Al ☐Ac
H55A	Hood 5				☐Al ☐Ac
ChemoA	Chemo Hood				☐Al ☐Ac
HorizA	Horizontal Hood				☐Al ☐Ac
H51TA	Table 2				☐Al ☐Ac
H52TA	Table 3				☐Al ☐Ac
H53TA	Table 4				☐Al ☐Ac
GownroomA	Gowning Area				☐Al ☐Ac
SinkA	Sink Area				☐Al ☐Ac
CrimpA	Crimping Bench				☐Al ☐Ac
MiddleroomA	Middle of Room				☐Al ☐Ac
NRNSA	Near Non-Sterile Lab				☐Al ☐Ac
1PrepA	Prep Room – Near Incubator				☐Al ☐Ac
2PrepA	Prep Room – Near Warehouse				☐Al ☐Ac

Alert		**Action**
1 CFU	ISO 4 (class 10) Glove box, Antechambers	2+ CFU
2 CFU	ISO 6 (class 1,000) Main Clean room	3+ CFU
5 CFU	ISO 7 (class 10,000) Gown room, Crimp room	8+ CFU
8 CFU	ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling:
Media Lot:
Exp Date:
Sampler Mfg/Model:
Serial #:
Calibration Due Date:

Quality Control: Date:
Reviewed By: Date:

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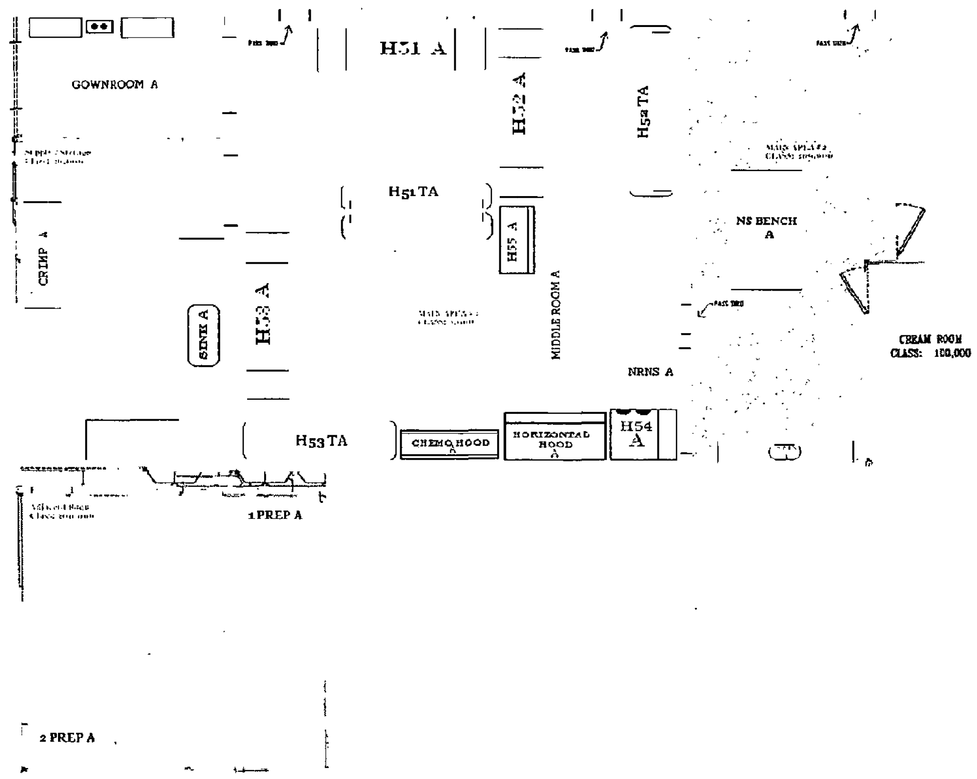
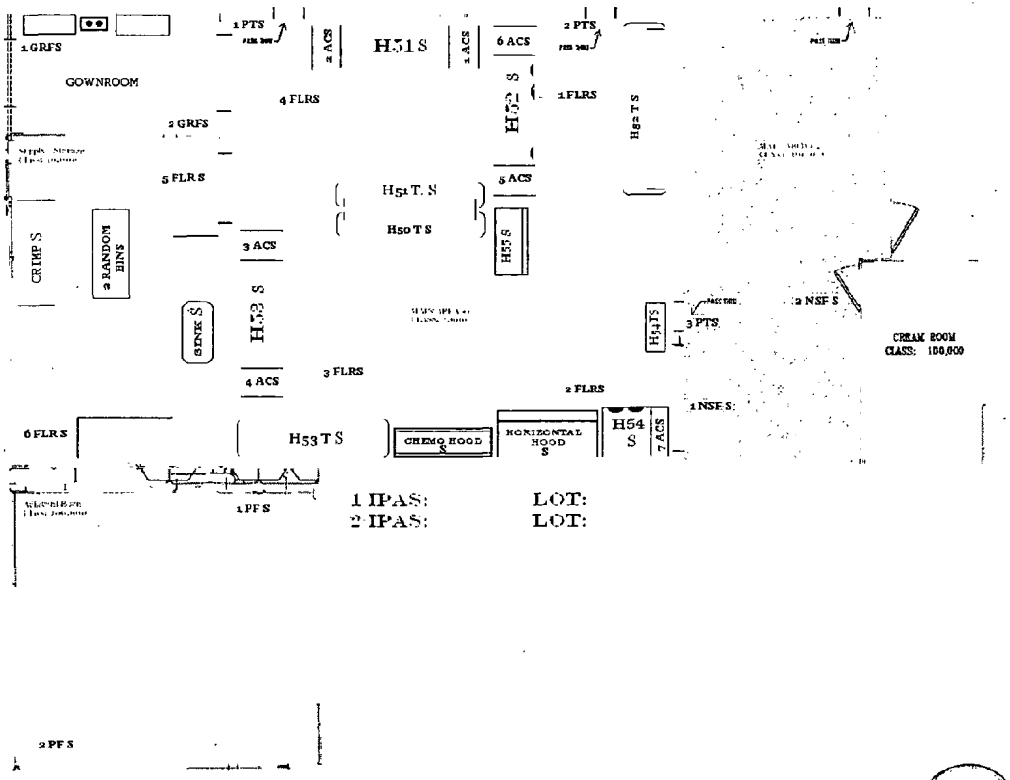
Clean Room Viable Air Sampling Diagram - Attachment 5



ORIGINAL
09-22-05

Clean Room Surface Sampling Diagram - Attachment 3



1 IPAS: LOT:
2 IPAS: LOT:

ORIGINAL
04-22-08

LEVELS FOR AIR AND SURFACE SAMPLING

ATTACHMENT 1

Note: ** Alert/Action Levels are to be determined after historical data is collected**

Levels for Air Sampling

Classifications	Alert Level	Action Level
ISO 4 (Class 10) Glove box, Antechambers	1 CFU	2+ CFU
ISO 6 (Class 1,000) Main Clean Room	2 CFU	4+ CFU / 9+ CFU (by hood 1)
ISO 7(Class 10,000) Gown room, Crimp Room	5 CFU	8+ CFU
ISO Class 8 (Class 100,000) Prep Room	8 CFU	10+ CFU

Levels for Surface Sampling

Classifications	Alert Level	Action Level
ISO 4 (Class 10) Glove box, antechambers	1 CFU	2+ CFU
ISO 6 (Class 1,000) Main Clean Room	3 CFU	5+ CFU
ISO 7(Class 10,000) ← Gown room, Crimp Room	5 CFU	7+ CFU
ISO Class 8 (Class 100,000) Prep Room	8 CFU	10+CFU

RECEIPT OF CONTACT PLATES
ATTACHMENT 2

Quantity Received	Manufacturer	Lot Number	Expiration Date	Received By (Initials/Date)	Incubation Dates of Positive and Negative Controls 30ºC-35ºC	Positive Control	Negative Control	Results (CFU)
					Incubation for 5 days at 30ºC-35ºC	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30ºC-35ºC	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30ºC-35ºC	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30ºC-35ºC	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30ºC-35ºC	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30ºC-35ºC	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject

Quality Control: **Date:**
Reviewed By: **Date:**

~~**Media Type**~~
~~**Manufacturer**~~
~~**Lot Number**~~
~~**Expiration Date**~~
~~**Received By (Initials/Date)**~~
~~**Incubation Dates Positive and Negative Controls**~~
~~**Positive Control**~~
~~**Negative Control**~~

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATES

ATTACHMENT 3

Media Lot # and Exp Date	Rph/Tech	Location and Product Being worked on	Incubation for 5 days at 30°C - 35°C	Results (CFU)	Alert / Action
Lot : Exp:			→		☐ Al ☐ Ac
Lot : Exp:			→		☐ Al ☐ Ac
Lot : Exp:			→		☐ Al ☐ Ac
Lot : Exp:			→		☐ Al ☐ Ac
Lot : Exp:			→		☐ Al ☐ Ac
Lot : Exp:			→		☐ Al ☐ Ac
Lot : Exp:			→		☐ Al ☐ Ac
Lot : Exp:			→		☐ Al ☐ Ac
Lot : Exp:			→		☐ Al ☐ Ac
Lot : Exp:			→		☐ Al ☐ Ac

Alert Level 1+ CFU
Action Level 2+ CFU

Quality Control: Date:

Reviewed By: Date:

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY		
SOP NUMBER: 3.030	**VERSION NUMBER: 5.0**	
Sterile Laboratory	Effective Date	10-21-11
Originator:		
Reviewer:		

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for viable and non-viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644-4 "Clean Rooms and Associated Controlled Environments", Part 4

4.4 SOP 3.010 "Sterile Compounding Area Requirements"

4.5 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.6 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Viable Particle - A viable particle is a particle that contains one or more living microorganisms.

5.3 Viable Air Sampler - Device used to sample microorganisms in the air.

5.4 Non-Viable Air Sampling - Total particle count. Includes viable particles but does not test for presence of microorganisms.

5.5 Surface Contact Plate - Agar plate used to sample surfaces for microorganisms by direct application. The agar contains neutralizers to inactivate residual disinfectants.

5.6 ISO Classifications

- 5.6.1 ISO Class 4 is equivalent to Class 10 (glove box, antechamber).
- 5.6.2 ISO Class 6 is equivalent to Class 1,000 (main clean room).
- 5.6.3 ISO Class 7 is equivalent to Class 10,000 (gown/crimp room).
- 5.6.4 ISO Class 8 is equivalent to Class 100,000 (prep room).

5.7 Alert Level - Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching alert level does not require investigation. (Attachment 1)

5.8 Action Level - Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action. (Attachment 1)

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled upon completion of sterile compounding and **prior to cleaning**.

6.2 Surface sampling in the glove boxes and antechambers Class 10(ISO Class 4), Class 1000 main clean room(ISO Class 6), Class10,000(ISO Class 7) gown/crimp room, Class100,000(ISO Class 8)prep room, area shall be performed weekly, **prior to cleaning**.

6.3 Sterility of 70% isopropyl alcohol (IPA) will be confirmed monthly.

6.4 Viable air sampling shall be performed every other week.

6.5 Non-Viable air sampling shall be performed at least every six months.

6.6 The Pharmacist-in-charge or the Quality Control officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 Viable air sampler with sterilized impeller and shroud (Model # SAS180)

7.4 Appropriate user manuals

7.5 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from "clean" areas to "dirty" areas.

9.0 PROCEDURE

9.1 Upon receipt of commercially prepared TSA contact plates, retain the manufacturer's Certificate of Analysis (CofA). Document receipt of the media on Receipt of Contact plates (Attachment 2).

9.2 Verify that the (CofA) documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

  9.2.1 Remove two plates from new lot of media received for positive and negative controls.

  9.2.2 Label one plate "Positive" and the other plate "Negative," and write the date on each plate.

  9.2.3 Do not expose the agar surface of the "Negative" plate. Seal the contact plate with parafilm.

  9.2.4 For the "Positive" control expose the agar to air for 15 minutes. Seal the contact plate with parafilm.

9.2.5 Incubate for 5 days at 30°C-35°C. Document on Attachment 2.

9.2.6 If the positive control has no growth or the negative control has growth, the lot must be rejected.

9.2.7 Place the completed Attachment 2, along with the (CofA) in a designated binder.

9.2.8 Store all acceptable media according to the manufacturer's recommendation in a monitored refrigerator. (2°C - 8°C).

9.3 Viable Air Sampling

9.3.1 Set up the air sampler according to the manufacturer's instructions.

9.3.2 Sanitize the exterior of the air sampler prior to use with a low-lint wipe, saturated with sterile 70% IPA.

9.3.3 If the sampler is being moved from a dirty to clean location during sampling, repeat exterior sanitization.

9.3.4 Make sure the air sampler is programmed with the following parameters:

Sample Time	Air Volume/Minute	Total Air Volume
5.5 Minutes	180 Liters	1000 liters (35ft^3)

9.3.5 Put on all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.3.6 Document all data on the appropriate attachments.

9.3.7 Obtain the appropriate quantity of media from storage.

9.3.7.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.3.7.2 Verify media is within expiration date and record media lot number and expiration date on Attachment 5.

9.3.7.3 Aseptically remove an agar contact plate from its package. Make sure that the contact plate covers remains on.

9.3.7.4 Aseptically remove the outer protective cap from the sampler and unscrew the aspirating head.

9.3.7.5 Secure the plate between the metal prongs. Once secure, remove the contact plate cover and immediately replace the aspirating head and screw on tightly.

NOTE: *Do not touch the agar surface (If agar is touched, discard the contact plate).*

9.3.8 Place the air sampler in the desired location at cart or bench top height. Orient the air sampler in a vertical position facing the ceiling and turn on.
Do not place arms over sampler while in operation.

9.3.8.1 The air sampler will automatically turn off at the conclusion of the sampling period.

9.3.8.2 Aseptically remove the contact plate from the sampler. Replace the lid of the contact plate.

9.3.8.2.1 Inspect the contact plate to ensure the impingement marks are present.

9.3.8.2.2 If impingement marks are not present, the sample is invalid and shall be repeated with a new contact plate.

9.3.8.3 Seal the contact plate with parafilm.

9.3.8.4 Record the site location on the base of the plate, initial and date. Do not record any information on the cover plate.

9.3.8.5 Invert the samples and incubate for as follows.

9.3.8.6 5 days at 30-35 °C.

NOTE: If 5th day of incubation falls on a non-business day, then the plates shall be incubated at that temperature for the remainder of the 7 days. Do not exceed 7 days of incubation.

NOTE: Samples may be shipped to a contract lab for incubation and analysis.

9.4 Non-Viable Air Sampling

9.4.1 Non-viable air sampling shall be performed every 6 months along with Room/Hood Certification.

9.4.2 Sampling shall be performed by an approved vendor using calibrated equipment.

9.4.3 File all completed documents in the designated binder.

9.5 Surface Sampling

9.5.1 Document all data on the appropriate attachments.

9.5.2 Surface sampling in the glove boxes and antechambers - Class 10 (ISO 4), Class 1000 (ISO 6) main clean room, Class 10,000 (ISO 7) gown/crimp room, Class 100,000 (ISO 8) prep room area shall be performed weekly, **prior to cleaning.**

9.5.3 Obtain the appropriate quantity of contact plates from storage.

9.5.3.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.5.3.2 Verify media is within expiration date and record media lot number and expiration date on appropriate attachment.

9.5.4 Put on all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.5.5 Sampling technique:

9.5.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Gently touch the agar to the desired surface and for 10 seconds.

9.5.5.2 Replace the cover and seal the plate with parafilm.

9.5.5.3 Record the site location on the base of the plate. Do not record any information on the cover of the plate.

9.5.5.4 Clean the sample site with sterile 70% IPA before proceeding to the next site.

9.5.6 Incubate for 5 days 30°C-35°C.

9.5.7 Record surface sampling results on Attachment 4, and file all completed documents in the EM binder.

9.6 Confirm the Sterility of 70% IPA

CLEAN Room Surface Sampling

9.6.1 Refer to the appropriate attachment for Surface Sampling ~~Log~~.

9.6.2 Obtain two contact plates from storage and test two random sterile 70% IPA bottles. This will be done monthly.

9.6.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.6.2.2 Verify media is within expiration date, and record media lot number and expiration date on Attachment ~~3~~ 4.

9.6.3 Aseptically remove the contact plate cover.

NOTE: *Do not touch the agar surface (If agar is touched, discard the contact plate).*

9.6.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.6.5 Replace the cover and seal the plate with parafilm.

9.6.6 Label the base of the plate with "IPA". Do not record any information on the cover of the plate.

9.6.7 Incubate for 5 days at 30°C-35°C.

9.6.8 Record results on Attachment 4, and file all completed documents in the EM binder.

9.7 Personnel Monitoring

9.7.1 Refer to the Clean Room Facility Personnel Touch Plates ~~Log~~ (Attachment 3).

9.7.2 Obtain the appropriate quantity of contact plates from storage.

9.7.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.7.2.2 Verify media is within expiration date.

9.7.2.3 Label the base of the contact plate with the date, the pharmacist/technician initials, the hand sampled and what product is being compounded.

9.7.2.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.7.3 Replace the cover and seal the plate with parafilm.

9.7.4 Incubate for 5 days at 30°C-35°C.

9.7.5 Record personnel monitoring results on Attachment 3, and file all completed documents in the EM binder.

9.8 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

9.9 Alert and Action Limits

9.9.1 Air Sampling (Viable)

9.9.2 Calculate the level of viable airborne particulates as CFU per cubic foot. The volume of air sampled in the Class 10 (ISO 4) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

9.9.2.1 The alert/action limits for air sampling should be derived from historical data. *** Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 1).**

9.9.3 Surface and Personnel Monitoring

9.9.3.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.9.3.2 The alert/action limits for surface and personnel monitoring should be derived from historical data. *** Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 1).**

9.10 Investigation and Corrective Actions

9.10.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

9.10.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized.

9.10.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.3.1 Review of sanitation procedures

9.10.3.2 Review of sampling technique

9.10.3.3 Review of clean room personnel

9.10.3.4 Inspection of sampling media

9.10.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.4.1 Identification of microbial isolates to determine origin

9.10.4.2 Review of pressure differential information

9.10.4.3 Review of HEPA and clean room certification

9.10.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.10.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

9.11 Reporting Results

9.11.1 Remove samples from the incubator. Record stop times on the appropriate attachment.

9.11.2 Count all colonies on the plate and document results for each category below.

- Bacteria
- Mold (Count or indicate presence)

- Total Counts of Bacteria and Mold combined

10.0 ATTACHMENTS

10.1 Attachment 1 - Levels for Air and Surface Sampling
10.2 Attachment 2 – Receipt of Contact Plates
10.3 Attachment 3 - Clean Room Facility Personnel Touch Plates
10. 5 Attachment 4 - Clean Room Surface Sampling
10.6 Attachment 5 – Clean Room Air Sampling
10.7 Attachment 6 - Clean Room Surface Diagram
10.8 Attachment 7 – Clean Room Air Diagram

1.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06012
2.0	04/06/06	Updated section 9.3 and attachment 1 to include positive/negative controls. Updated sample identification labels and schematic maps on attachments 2, 3, 4 and 5.	CR06053
3.0	11/30/07	Taking out TSA Strips, non-viable samples, fixing iso/ classes not correct	CR07018
4.0	09-22-08	Re did attachments for new clean room, Minor changes	CR08017
5.0	10-21-11	Need to update with our move to a new clean room	CR11011

5.7 Alert Level -Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching alert level does not require investigation. (Attachment 8)

5.8 Action Level - Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action. (Attachment 8)

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled upon completion of sterile compounding and **prior to cleaning**.

6.2 Surface sampling in the glove boxes and antechambers Class 10(ISO Class 4), Class 1000 main clean room(ISO Class 6), Class10,000(ISO Class 7) gown/crimp room, Class100,000(ISO Class 8)prep room, area shall be performed weekly, **prior to cleaning**.

6.3 Sterility of 70% isopropyl alcohol (IPA) will be confirmed ~~weekly~~ Monthly.

6.4 Viable air sampling shall be performed ~~weekly~~. every other week

6.5 Non-Viable air sampling shall be performed at least every six months.

6.6 The Pharmacist-in-charge or the Quality Control officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 Viable air sampler with sterilized impeller and shroud (Model # SAS180)

7.4 Appropriate user manuals

7.5 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from "clean" areas to "dirty" areas.

9.0 PROCEDURE

9.1 Upon receipt of commercially prepared TSA contact plates, retain the manufacturer's Certificate of Analysis (CofA). Document receipt of the media on Receipt of Contact plates (Attachment 1).

9.2 Verify that the (CofA) documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

  9.2.1 Remove two plates from new lot of media received for positive and negative controls.

  9.2.2 Label one plate "Positive" and the other plate "Negative," and write the date on each plate.

  9.2.3 Do not expose the agar surface of the "Negative" plate. Seal the contact plate with parafilm.

  9.2.4 For the "Positive" control expose the agar to air for 15 minutes. Seal the contact plate with parafilm.

  9.2.5 Incubate for 5 days at 30°C-35°C. Document on Attachment 1.

ORIGINAL
09-22-08

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY	
SOP NUMBER: 3.030	**VERSION NUMBER: 4.0**
Sterile Laboratory	Effective Date 09-22-08
Originator:	
Reviewer:	

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for viable and non-viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644-4 "Clean Rooms and Associated Controlled Environments", Part 4

4.4 SOP 3.010 "Sterile Compounding Area Requirements"

4.5 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.6 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Viable Particle - A viable particle is a particle that contains one or more living microorganisms.

5.3 Viable Air Sampler - Device used to sample microorganisms in the air.

5.4 Non-Viable Air Sampling - Total particle count. Includes viable particles but does not test for presence of microorganisms.

5.5 Surface Contact Plate - Agar plate used to sample surfaces for microorganisms by direct application. The agar contains neutralizers to inactivate residual disinfectants.

5.6 ISO Classifications

  5.6.1 ISO Class 4 is equivalent to Class 10 (glove box, antechamber).

  5.6.2 ISO Class 6 is equivalent to Class 1,000 (main clean room).

  5.6.3 ISO Class 7 is equivalent to Class 10,000 (gown/crimp room).

  4.1.1 ISO Class 8 is equivalent to Class 100,000 (prep room).

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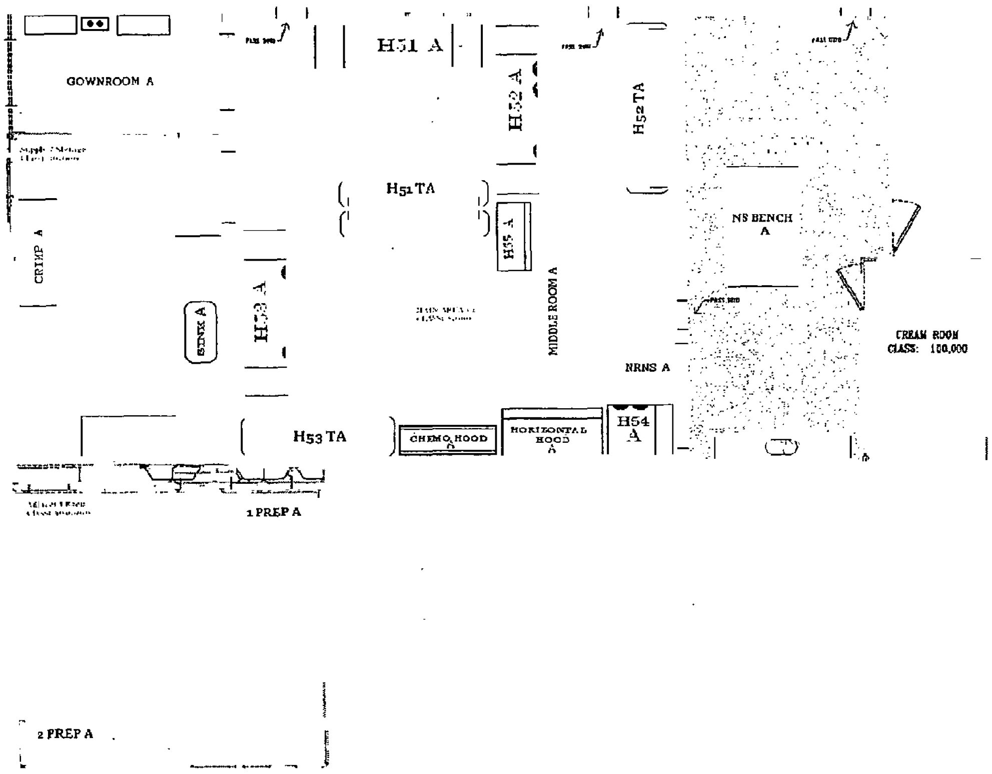
9-22-08

Clean Room Viable Air Sampling Diagram - Attachment 5



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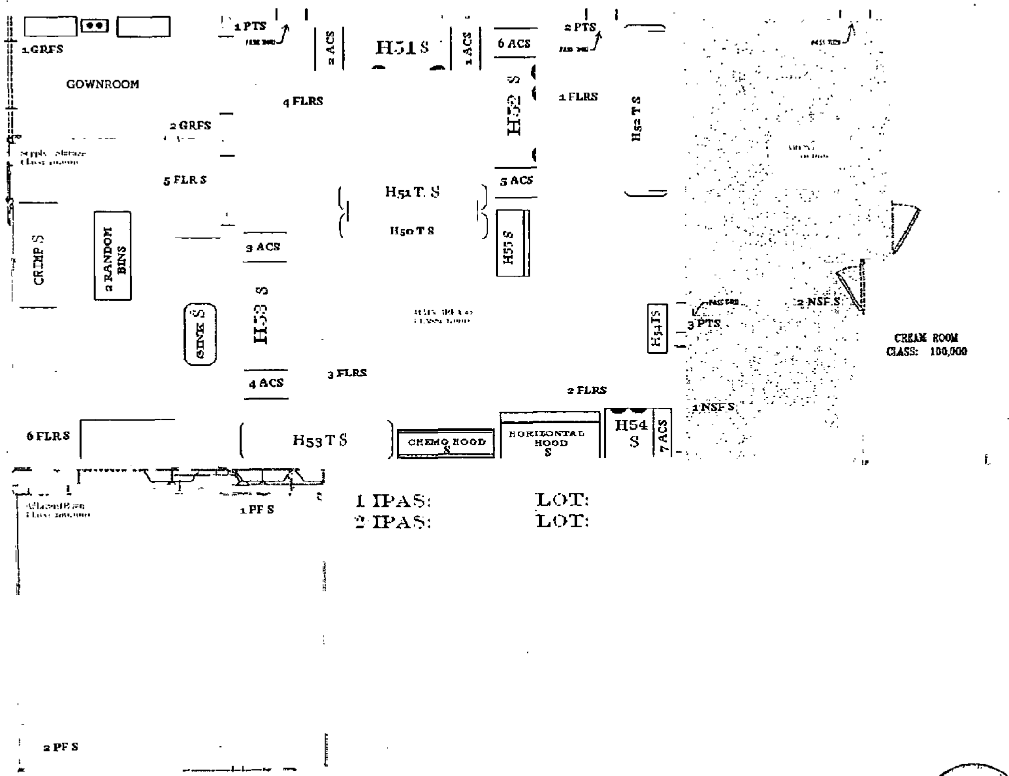
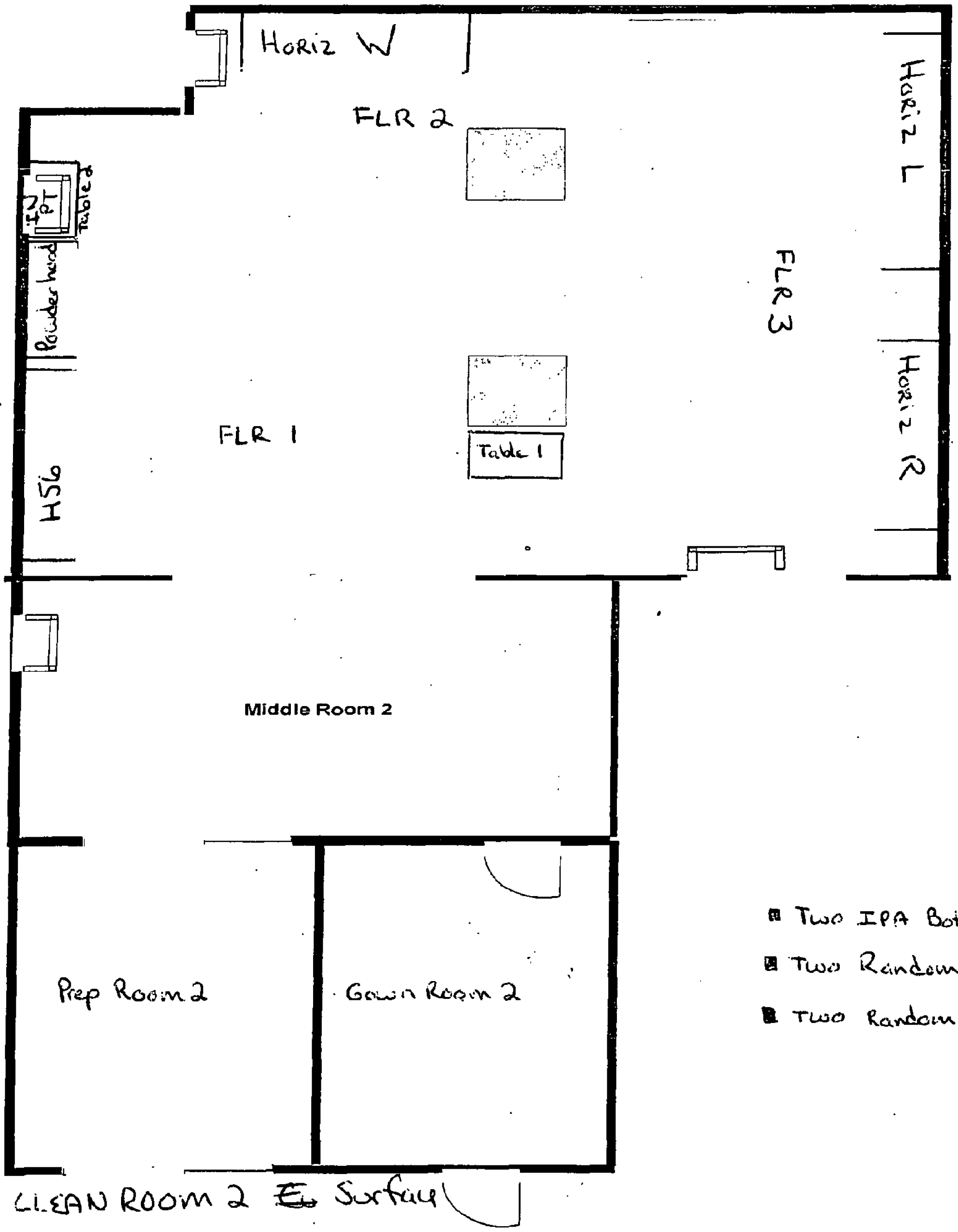
09-22-05

Clean Room Surface Sampling Diagram - Attachment 3



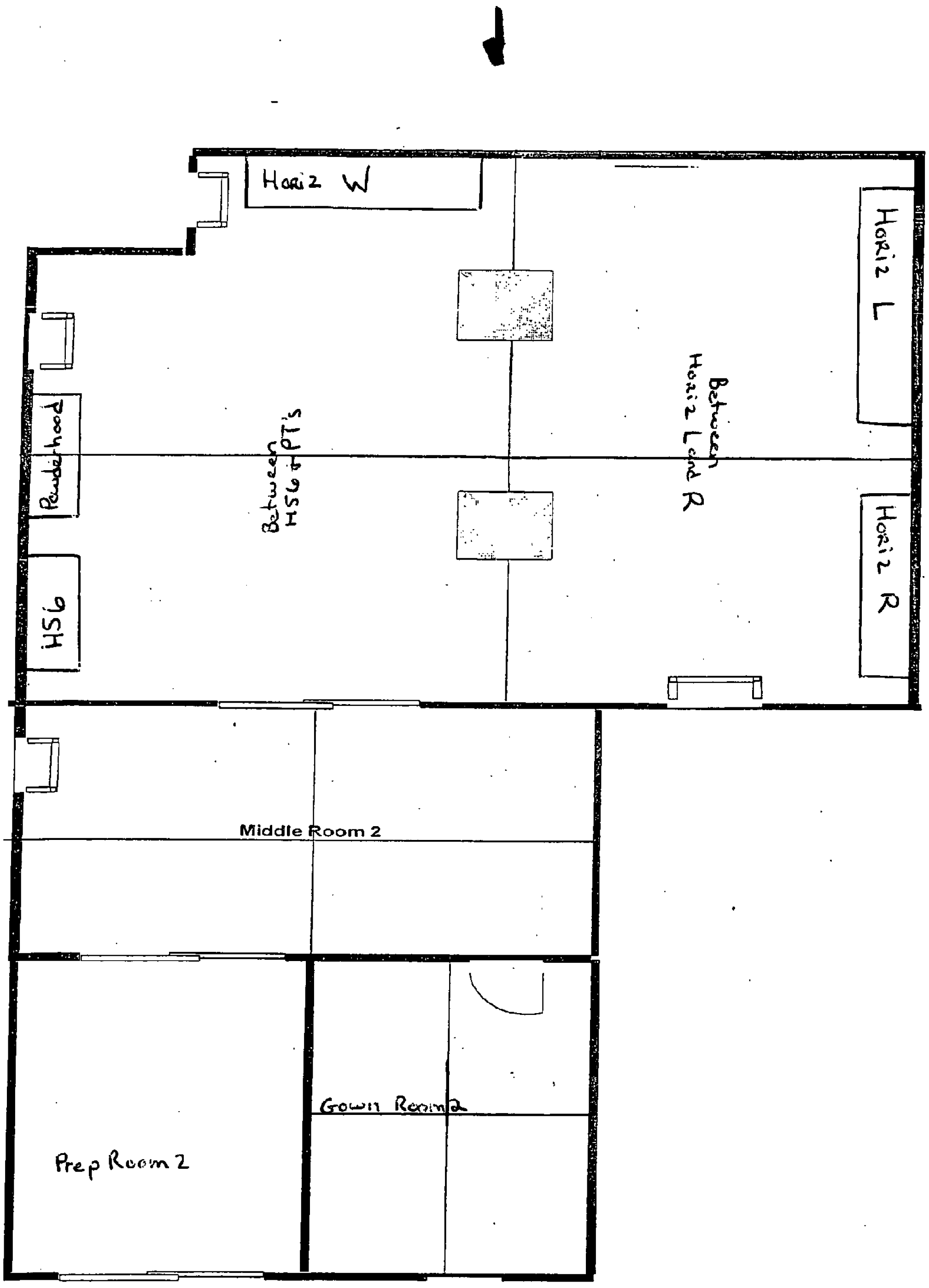
1 IPAS: LOT:
2 IPAS: LOT:

ORIGINAL
04-22-08



CLEAN ROOM 2 ~~E~~ Surface

▦ Two IPA Bottles once a month
▨ Two Random Bin's
■ Two Random Wall



CLEAN ROOM 2 AIR

change CFU on Air from 2+ to 3+

Add walls to EM

3.030

SOP NEW/CHANGE REQUEST FORM – Attachment 1

(Page 1 of 2)

Check one: ☐ New ☑ Change **Change Request Log Number:** 11011

SOP Number/Title: 3.030 Environmental Monitoring of the Clean Room Facility

Version of SOP being changed: 4.0 **New Version:** 5.0

Description/Text of Change: (see attached Changed Document)

Reason for Change Request: Different clean room – need to update w/ our Move

Supporting Documentation: (mark one)

☑ None Required ☐ Attached → reference (specify):

Requested Implementation Date: (mark one)

☐ Less than 30 Days ☐ By Date:

Annual SOP Review Requirements: (mark one)

☑ Complete review was performed to satisfy the requirements of SOP review (see page 2).

☐ Review limited to changes only, SOP review will need to be performed when scheduled.

Check Training Requirements: (mark one)

☑ Read and Understand Memo ☐ Training Session Required

Training Checklist:

☐ No Checklist is Required **OR** TC# has been reviewed and:

☐ No Changes are Required

☐ Checklist needs to be Written/Changes are Required → TC change #

Change Originator: Printed Name Signature Date

Quality Control: Printed Name Signature Date

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11-207

SOP REVIEW FORM – Attachment 1

(Page 2 of 2)

SOP Number/Title: 3-030 Environmental Monitoring of the Clean Room Facility

Date Effective: 09-22-08 **Version:** 4.0 **Last Reviewed:** 02-15-10

SOP REVIEW – PLEASE CHECK THE FOLLOWING AS THEY ARE PERFORMED:

- ☑ Ensure that the purpose, scope, responsibilities, definitions, and general information sections are still accurate and current.
- ☑ Ensure that the responsible functional area groups are consistent with current organizational structure.
- ☑ Check references to ensure that they still apply, that the titles have not changed, and that the references to documents within the text are correct.
- ☑ Verify that all materials, equipment, reagents, etc. called for in the procedure are still available and are being used.
- ☑ Ensure that the current practice is reflected accurately in the procedure section of the SOP.
- ☑ Ensure that the procedure addresses what action to take if the task has unacceptable results.
- ☑ Ensure that all documentation requirements and storage/archival requirements are reflected in the SOP.
- ☑ Ensure that all attachments continue to be accurate and reflect current practices.

CHOOSE THE STATEMENT THAT APPLIES:

I have reviewed the above mentioned procedure and:

- ☐ No changes need to be implemented.
- ☑ SOP New/Change Request Form is attached to update the procedure, Change Request Log Number CR 11011.
- ☐ SOP should be deactivated, Change Request Log Number CR__________.

SOP Review Performed By: __________ Date: 08-15-11

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9.2.6 If the positive control has no growth or the negative control has growth, the lot must be rejected.

9.2.7 Place the completed Attachment 1, along with the (CofA) in a designated binder.

9.2.8 Store all acceptable media according to the manufacturer's recommendation in a monitored refrigerator. (2°C - 8°C).

9.3 Viable Air Sampling

9.3.1 Set up the air sampler according to the manufacturer's instructions.

9.3.2 Sanitize the exterior of the air sampler prior to use with a low-lint wipe, saturated with sterile 70% IPA.

9.3.3 If the sampler is being moved from a dirty to clean location during sampling, repeat exterior sanitization.

9.3.4 Make sure the air sampler is programmed with the following parameters:

Sample Time	Air Volume/Minute	Total Air Volume
5.5 Minutes	180 Liters	1000 liters (35ft³)

9.3.5 ~~Don~~ all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.3.6 Document all data on the appropriate Attachments.

9.3.7 Obtain the appropriate quantity of media from storage.

9.3.7.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.3.7.2 Verify media is within expiration date and record media lot number and expiration date on Attachment 6.

9.3.7.3 Aseptically remove an agar contact plate from its package. Make sure that the contact plate covers remains on.

9.3.7.4 Aseptically remove the outer protective cap from the sampler and unscrew the aspirating head.

9.3.7.5 Secure the plate between the metal prongs. Once secure, remove the contact plate cover and immediately replace the aspirating head and screw on tightly.

NOTE: *Do not touch the agar surface (If agar is touched, discard the contact plate).*

9.3.8 Place the air sampler in the desired location at cart or bench top height. Orient the air sampler in a vertical position facing the ceiling and turn on.
Do not place arms over sampler while in operation.

9.3.8.1 The air sampler will automatically turn off at the conclusion of the sampling period.

9.3.8.2 Aseptically remove the contact plate from the sampler. Replace the lid of the contact plate.

9.3.8.2.1 Inspect the contact plate to ensure the impingement marks are present.

9.3.8.2.2 If impingement marks are not present, the sample is invalid and shall be repeated with a new contact plate.

9.3.8.3 Seal the contact plate with parafilm.

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04-22-08

9.3.8.4 Record the site location on the base of the plate, initial and date. Do not record any information on the cover plate.

9.3.8.5 Invert the samples and incubate for as follows.

9.3.8.6 5 days at 30-35 °C.

NOTE: If 5th day of incubation falls on a non-business day, then the plates shall be incubated at that temperature for the remainder of the 7 days. Do not exceed 7 days of incubation.

NOTE: Samples may be shipped to a contract lab for incubation and analysis.

9.4 Non-Viable Air Sampling

9.4.1 Non-viable air sampling shall be performed every 6 months along with Room/Hood Certification.

9.4.2 Sampling shall be performed by an approved vendor using calibrated equipment.

9.4.3 File all completed documents in the designated binder.

9.5 Surface Sampling

9.5.1 Document all data on the appropriate Attachments.

9.5.2 Surface sampling in the glove boxes and antechambers - Class 10 (ISO 4), Class 1000 (ISO 6)main clean room, Class 10,000 (ISO 7)gown/crimp room, Class 100,000 (ISO 8) prep room area shall be performed weekly, **prior to cleaning**

9.5.3 Obtain the appropriate quantity of contact plates from storage.

9.5.3.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.5.3.2 Verify media is within expiration date and record media lot number and expiration date on appropriate Attachment.

9.5.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.5.5 Sampling technique:

9.5.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface for 10 seconds.

9.5.5.2 Replace the cover and seal the plate with parafilm.

9.5.5.3 Record the site location on the base of the plate. Do not record any information on the cover of the plate.

9.5.5.4 Clean the sample site with sterile 70% IPA before proceeding to the next site.

9.5.6 Incubate for 5 days 30°C-35°C.

9.5.7 Record surface sampling results on Attachment 2, and file all completed documents in the EM binder.

9.6 Confirm the Sterility of 70% IPA

9.6.1 Refer to the appropriate Attachment for Surface Sampling Log

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04-22-08

9.6.2 Obtain two contact plates from storage and test two random sterile 70% IPA bottles.

9.6.2.1 Inspect each plate and discard any damaged or contaminated media and replace. This will be done monthly

9.6.2.2 Verify media is within expiration date, and record media lot number and expiration date on Attachment 2. --- - This

9.6.3 Aseptically remove the contact plate cover.

NOTE: *Do not touch the agar surface (If agar is touched, discard the contact plate).*

9.6.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.6.5 Replace the cover and seal the plate with parafilm.

9.6.6 Label the base of the plate with "IPA" ~~and the IPA lot number/expiration date~~. Do not record any information on the cover of the plate.

9.6.7 Incubate for 5 days at 30°C-35°C.

9.6.8 Record results on Attachment 2, and file all completed documents in the EM binder.

9.7 Personnel Monitoring

9.7.1 Refer to the Clean Room Facility Personnel Touch Plate Log (Attachment 3).

9.7.2 Obtain the appropriate quantity of contact plates from storage.

9.7.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.7.2.2 Verify media is within expiration date.

9.7.2.3 Label the base of the contact plate with the date, the pharmacist/technician initials, the hand sampled and what product is being compounded.

9.7.2.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.7.3 Replace the cover and seal the plate with parafilm.

9.7.4 Incubate for 5 days at 30°C-35°C.

9.7.5 Record personnel monitoring results on Attachment 3 and file all completed documents in the EM binder.

9.8 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

9.9 Alert and Action Limits

9.9.1 Air Sampling (Viable)

9.9.2 Calculate the level of viable airborne particulates as CFU per cubic foot. The volume of air sampled in the Class 10 (ISO 4) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

9.9.2.1 The alert/action limits for air sampling should be derived from historical data. * **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 8).**

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RANDOM AIR/SURFACE SAMPLING - ATTACHMENT 4

Air/Surface Sample Location	**Description**	**Results**		
		Bacteria CFU	*Mold CFU*	*Total CFU*

Date of Sampling:
Media Lot#: Exp Date:
Sampler Mfg/Model: Calibration Due Date:

Quality Control: Date:

Reviewed By: Date:

ORIGINAL
09-22-08

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY
SOP NUMBER: 3.030 **VERSION NUMBER: 4.0**

LEVELS FOR AIR AND SURFACE MONITORING - ATTACHMENT ~~8~~ 1

*Note: ** Alert/Action Levels are to be determined after historical data is collected***

Levels for Air Sampling

Classifications	Alert Level	Action Level
ISO 4 (Class 10) Glove box, Antechambers	1 CFU	2+ CFU
ISO 6 (Class 1,000) Main Clean Room	2 CFU	~~4~~3+ CFU / by hood 1 9+
ISO 7(Class 10,000) Gown room, Crimp Room	5 CFU	8+ CFU
ISO Class 8 (Class 100,000) Prep Room	8 CFU	10+ CFU

Levels for Surface Sampling

Classifications			Alert Level	Action Level
ISO 4 (Class 10) Glove box, Antechambers			1 CFU	2+ CFU
ISO 6 (Class 1,000) Main Clean Room			3 CFU	5+ CFU / ~~by hood~~ [illegible]
ISO 7(Class 10,000) Gown room, Crimp Room			5 CFU	7+ CFU
ISO Class 8 (Class 100,000) Prep Room			8 CFU	10+CFU

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CLEAN ROOM VIABLE AIR SAMPLING - ATTACHMENT 6

Page 1 of 1

Sample Location	Description	Results Bacteria CFU	 Mold CFU	 Total CFU	Alert/Action
H51A	Hood 1				☐Al ☐Ac
H52A	Hood 2				☐Al ☐Ac
H53A	Hood 3				☐Al ☐Ac
H54A	Hood 4				☐Al ☐Ac
H55A	Hood 5				☐Al ☐Ac
ChemoA	Chemo Hood				☐Al ☐Ac
HorizA	Horizontal Hood				☐Al ☐Ac
H51TA	Table 2				☐Al ☐Ac
H52TA	Table 3				☐Al ☐Ac
H53TA	Table 4				☐Al ☐Ac
GownroomA	Gowning Area				☐Al ☐Ac
SinkA	Sink Area				☐Al ☐Ac
CrimpA	Crimping Bench				☐Al ☐Ac
MiddleroomA	Middle of Room				☐Al ☐Ac
NRNSA	Near Non-Sterile Lab				☐Al ☐Ac
1PrepA	Prep Room – Near Incubator				☐Al ☐Ac
2PrepA	Prep Room – Near Warehouse				☐Al ☐Ac

Alert		**Action**
1 CFU	ISO 4 (class 10) Glove box, Antechambers	2+ CFU
2 CFU	ISO 6 (class 1,000) Main Clean room	3+ CFU
5 CFU	ISO 7 (class 10,000) Gown room, Crimp room	8+ CFU
8 CFU	ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling:
Sampler Mfg/Model:
Media Lot:
Serial #:
Exp Date:
Calibration Due Date:

Quality Control: Date:
Reviewed By: Date:

CLEAN ROOM SURFACE SAMPLING - ATTACHMENT 2

(Page 2 of 2)

Sample Location	Description	Results *Bacteria CFU*	*Mold CFU*	*Total CFU*	Alert/ Action
SinkS	Sink in Crimp Room				☐Al ☐Ac
CrimpS	Crimping Bench				☐Al ☐Ac
1RBS	Random Bin				☐Al ☐Ac
2RBS	Random Bin				☐Al ☐Ac
1GRFS	Gown Room – Near Hall				☐Al ☐Ac
2GRFS	Gown Room – Near Clean room				☐Al ☐Ac
1PFS	Prep Room – Near Incubator				☐Al ☐Ac
2PFS	Prep Room – Near Warehouse				☐Al ☐Ac
1FLRS	Clean Room Floor				☐Al ☐Ac
2FLRS	Clean Room Floor				☐Al ☐Ac
3FLRS	Clean Room Floor				☐Al ☐Ac
4FLRS	Clean Room Floor				☐Al ☐Ac
5FLRS	Clean Room Floor				☐Al ☐Ac
6FLRS	Clean Room Floor				☐Al ☐Ac
1IPAS	Isopropyl Alcohol				☐Al ☐Ac
2IPAS	Isopropyl Alcohol				☐Al ☐Ac

Alert		**Action**
1 CFU	ISO 4 (class 10) Glove box, Antechambers	2+ CFU
3 CFU	ISO 6 (class 1,000) Main Clean room	5+ CFU
5 CFU	ISO 7 (class 10,000) Gown room, Crimp room	7+ CFU
8 CFU	ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling:
Media Lot:
Exp Date:

Quality Control:
Date:

Reviewed By:
Date:

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04-22-08

CLEAN ROOM SURFACE SAMPLING - ATTACHMENT 2

(Page 1 of 2)

Sample Location	Description	Results			Alert/ Action
		Bacteria CFU	*Mold CFU*	*Total CFU*	
H51S	Hood 1				☐Al ☐Ac
H52S	Hood 2				☐Al ☐Ac
H53S	Hood 3				☐Al ☐Ac
H54S	Hood 4				☐Al ☐Ac
H55S	Hood 5				☐Al ☐Ac
1ACS	Hood 1 Antechamber (Right Side)				☐Al ☐Ac
2ACS	Hood 1 Antechamber (Left Side)				☐Al ☐Ac
3ACS	Hood 2 Antechamber (Right Side)				☐Al ☐Ac
4ACS	Hood 2 Antechamber (Left Side)				☐Al ☐Ac
5ACS	Hood 3 Antechamber (Left Side)				☐Al ☐Ac
6ACS	Hood 3 Antechamber (Right Side)				☐Al ☐Ac
7ACS	Hood 4 Antechamber				☐Al ☐Ac
ChemoS	Chemo Hood				☐Al ☐Ac
HorizS	Horizontal Hood				☐Al ☐Ac
H50TS	Table 1				☐Al ☐Ac
H51TS	Table 2				☐Al ☐Ac
H52TS	Table 3				☐Al ☐Ac
H53TS	Table 4				☐Al ☐Ac
H54TS	Table 5				☐Al ☐Ac
1PTS	Pass - thru				☐Al ☐Ac
2PTS	Pass - thru				☐Al ☐Ac
3PTS	Pass - thru				☐Al ☐Ac

ORIGINAL
04-22-08

RECEIPT OF CONTACT PLATES - ATTACHMENT ~~A~~ 2

Quantity Rec'd (i.e. boxes of 50 plates)	*Manufacturer*	*Lot Number*	*Expiration Date*	*Received By (Initials/Date)*	*Incubation Dates of Positive and Negative Controls 30°C-35°C*	*Positive Control*	*Negative Control*	*Results (CFU)*
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth.	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject

Quality Control: Date:
Reviewed By: Date:

ORIGINAL
AWK
04-22-08

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATE LOG - ATTACHMENT ~~7~~ 3

Media Lot # and Exp Date	Rph/Tech	Location and Product Being worked on	Incubation for 5 days at 30ºC - 35ºC	Results (CFU)	Alert / Action
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac

Alert Level 1+ CFU
Action Level 2+ CFU

Quality Control: Date:

Reviewed By: Date:

ORIGINAL
09-3-2005

9.12.1 Remove samples from the incubator. Record stop times on the appropriate attachment.

9.12.2 Count all colonies on the plate and document results for each category below.

- Bacteria
- Mold (Count or indicate presence)
- Total Counts of Bacteria and Mold combined

10.0 ATTACHMENTS

10.1 Attachment 1 - Receipt of Contact Plates
10.2 Attachment 2 - Clean Room Surface Sampling
10.3 Attachment 3 - Clean Room Surface Sampling Diagram
10.4 Attachment 4 - Random Air/Surface Sample Form
10.5 Attachment 5 - Clean Room Viable Air Sampling Diagram
10.6 Attachment 6 - Clean Room Viable Air Sampling
10.7 Attachment 7 - Clean Room Facility Personnel Touch Plate Log
10.8 Attachment 8 - Levels for Air and Surface Monitoring

1.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06012
2.0	04/06/06	Updated section 9.3 and attachment 1 to include positive/negative controls. Updated sample identification labels and schematic maps on attachments 2, 3, 4 and 5.	CR06053
3.0	11/30/07	Taking out TSA Strips, non-viable samples, fixing iso/ classes not correct	CR07018
4.0	09-22-08	Re did attachments for new clean room, Minor changes	CR08017

ORIGINAL

9.9.3 Surface and Personnel Monitoring

9.9.3.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.9.3.2 The alert/action limits for surface and personnel monitoring should be derived from historical data. * **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 8).**

9.10 Investigation and Corrective Actions

9.10.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

9.10.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized.

9.10.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.3.1 Review of sanitation procedures

9.10.3.2 Review of sampling technique

9.10.3.3 Review of clean room personnel

9.10.3.4 Inspection of sampling media

9.10.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.4.1 Identification of microbial isolates to determine origin

9.10.4.2 Review of pressure differential information

9.10.4.3 Review of HEPA and clean room certification

9.10.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.10.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

9.11 Non-Routine Samples

9.11.1 Non-routine samples that are not listed on the Viable and Surface Sampling Forms may be taken at a desired location.

9.11.2 Take the sample according to the appropriate air or surface sampling procedure above.

9.11.3 Document air/surface sample location and results on Attachment 4.

9.11.4 Non-routine samples are investigational and shall not be compared to alert/action values. Do not generate an alert or action as described in 9.10 for non-routine samples

9.12 Reporting Results

ORIGINAL

Surfac
~~ASI~~ ✓
~~Passthrough~~ ✓
~~In PT.~~ ✓
~~Horiz LW~~ ✓
~~Horiz L~~ ✓
~~Horiz R~~ ✓
~~table 1~~ ✓
~~table 2~~ ✓
1 FLR –
~~2 FLR~~ –
~~3 FLR~~ –
~~Middleroom~~ FLR ✓

~~[illegible]~~
IPA every month

4 FLR middleroom
N
5 Gownroom ✓
6 Prep ✓

2 walls
2 Bins
2
Prep Room FLR
Gownroom FLR

SOP REVIEW FORM

(Page 2 of 2)

SOP Number/Title: 3030 Enviro· Environmental Monitoring of the Clean Room Facility

Date Effective: 09-22-08 **Version:** 4.0 **Last Reviewed:** 02-15-10

SOP REVIEW – PLEASE CHECK THE FOLLOWING AS THEY ARE PERFORMED:

- ☐ Ensure that the purpose, scope, responsibilities, definitions, and general information sections are still accurate and current.
- ☐ Ensure that the responsible functional area groups are consistent with current organizational structure.
- ☐ Check references to ensure that they still apply, that the titles have not changed, and that the references to documents within the text are correct.
- ☐ Verify that all materials, equipment, reagents, etc. called for in the procedure are still available and are being used.
- ☐ Ensure that the current practice is reflected accurately in the procedure section of the SOP.
- ☐ Ensure that the procedure addresses what action to take if the task has unacceptable results.
- ☐ Ensure that all documentation requirements and storage/archival requirements are reflected in the SOP.
- ☐ Ensure that all attachments continue to be accurate and reflect current practices.

CHOOSE THE STATEMENT THAT APPLIES:

I have reviewed the above mentioned procedure and:

- ☐ No changes need to be implemented.
- ☐ SOP New/Change Request Form is attached to update the procedure, Change Request Log Number CR
- ☐ SOP should be deactivated, Change Request Log Number CR

SOP Review Performed By: **Date:**

ORIGINAL

SOP NEW/CHANGE REQUEST FORM

(Page 1 of 2)

Check one: ☐ New ☐ Change **Change Request Log Number:**

SOP Number/Title:

Version of SOP being changed: **New Version:**

Description/Text of Change: (see attached Changed Document)

Reason for Change Request:

Supporting Documentation: (mark one)

☐ None Required ☐ Attached → reference (specify):

Requested Implementation Date: (mark one)

☐ Less than 30 Days ☐ By Date:

Annual SOP Review Requirements: (mark one)

☐ Complete review was performed to satisfy the requirements of SOP review (see page 2).

☐ Review limited to changes only. SOP review will need to be performed when scheduled.

Check Training Requirements: (mark one)

☐ Read and Understand Memo ☐ Training Session Required

Training Checklist:

☐ No Checklist is Required OR TC#__________ has been reviewed and:

☐ No Changes are Required

☐ Checklist needs to be Written/Changes are Required → TC change #

Change Originator:	Printed Name	Signature	Date
Quality Control:	Printed Name	Signature	Date

ORIGINAL

SOP REVIEW FORM

(Page 2 of 2)

SOP Number/Title: 3-030 Enviromental Monitoring of the clean Room Facility

Date Effective: 09-22-08 **Version:** 4.0 **Last Reviewed:** 01-28-09

SOP REVIEW - PLEASE CHECK THE FOLLOWING AS THEY ARE PERFORMED:

- ☒ Ensure that the purpose, scope, responsibilities, definitions, and general information sections are still accurate and current.
- ☒ Ensure that the responsible functional area groups are consistent with current organizational structure.
- ☒ Check references to ensure that they still apply, that the titles have not changed, and that the references to documents within the text are correct.
- ☒ Verify that all materials, equipment, reagents, etc. called for in the procedure are still available and are being used.
- ☒ Ensure that the current practice is reflected accurately in the procedure section of the SOP.
- ☒ Ensure that the procedure addresses what action to take if the task has unacceptable results.
- ☒ Ensure that all documentation requirements and storage/archival requirements are reflected in the SOP.
- ☒ Ensure that all attachments continue to be accurate and reflect current practices.

CHOOSE THE STATEMENT THAT APPLIES:

I have reviewed the above mentioned procedure and:

- ☒ No changes need to be implemented.
- ☐ SOP New/Change Request Form is attached to update the procedure, Change Request Log Number CR
- ☐ SOP should be deactivated, Change Request Log Number CR

SOP Review Performed By: Annette Robe[illegible] **Date:** 02-15-10

ORIGINAL

SOP 1.010 New England Compounding Center Version 2.0

Attachment 1

SOP NEW/CHANGE REQUEST FORM

(Page 1 of 2)

Check one: ☐ New ☐ Change **Change Request Log Number:**

SOP Number/Title:

Version of SOP being changed: **New Version:**

Description/Text of Change: (see attached Changed Document)

Reason for Change Request:

Supporting Documentation: (mark one)

☐ None Required ☐ Attached → reference (specify):

Requested Implementation Date: (mark one)

☐ Less than 30 Days ☐ By Date:

Annual SOP Review Requirements: (mark one)

☐ Complete review was performed to satisfy the requirements of SOP review (see page 2).

☐ Review limited to changes only. SOP review will need to be performed when scheduled.

Check Training Requirements: (mark one)

☐ Read and Understand Memo ☐ Training Session Required

Training Checklist:

☐ No Checklist is Required OR TC#__________ has been reviewed and:

☐ No Changes are Required

☐ Checklist needs to be Written/Changes are Required → TC change #

02-15-10

Change Originator: Printed Name Signature ________ Date

Quality Control: Printed Name Signature ________ Date

ORIGINAL

SOP 1.010 New England Compounding Center Version 2.0

Attachment 1

SOP REVIEW FORM

(Page 2 of 2)

SOP Number/Title: 3.030 Environmental Monitoring of the Clean Room Facility

Date Effective: 09-22-08 **Version:** 4.0 **Last Reviewed:** 03-08-07

SOP REVIEW – PLEASE CHECK THE FOLLOWING AS THEY ARE PERFORMED:

- ☐ Ensure that the purpose, scope, responsibilities, definitions, and general information sections are still accurate and current.
- ☐ Ensure that the responsible functional area groups are consistent with current organizational structure.
- ☐ Check references to ensure that they still apply, that the titles have not changed, and that the references to documents within the text are correct.
- ☐ Verify that all materials, equipment, reagents, etc. called for in the procedure are still available and are being used.
- ☐ Ensure that the current practice is reflected accurately in the procedure section of the SOP.
- ☐ Ensure that the procedure addresses what action to take if the task has unacceptable results.
- ☐ Ensure that all documentation requirements and storage/archival requirements are reflected in the SOP.
- ☐ Ensure that all attachments continue to be accurate and reflect current practices.

CHOOSE THE STATEMENT THAT APPLIES:

I have reviewed the above mentioned procedure and:

- ☐ No changes need to be implemented.
- ☐ SOP New/Change Request Form is attached to update the procedure, Change Request Log Number CR
- ☐ SOP should be deactivated, Change Request Log Number CR

SOP Review Performed By: Annette Robin **Date:** 01-28-09

ORIGINAL

SOP NEW/CHANGE REQUEST FORM

(Page 1 of 2)

Check one: ☐ New ☐ Change **Change Request Log Number:**

SOP Number/Title:

Version of SOP being changed: **New Version:**

Description/Text of Change: (see attached Changed Document)

Reason for Change Request:

Supporting Documentation: (mark one)

☐ None Required ☐ Attached → reference (specify):

Requested Implementation Date: (mark one)

☐ Less than 30 Days ☐ By Date:

Annual SOP Review Requirements: (mark one)

☐ Complete review was performed to satisfy the requirements of SOP review (see page 2).

☐ Review limited to changes only, SOP review will need to be performed when scheduled.

Check Training Requirements: (mark one)

☐ Read and Understand Memo ☐ Training Session Required

Training Checklist:

☐ No Checklist is Required **OR** TC#__________ has been reviewed and:

☐ No Changes are Required

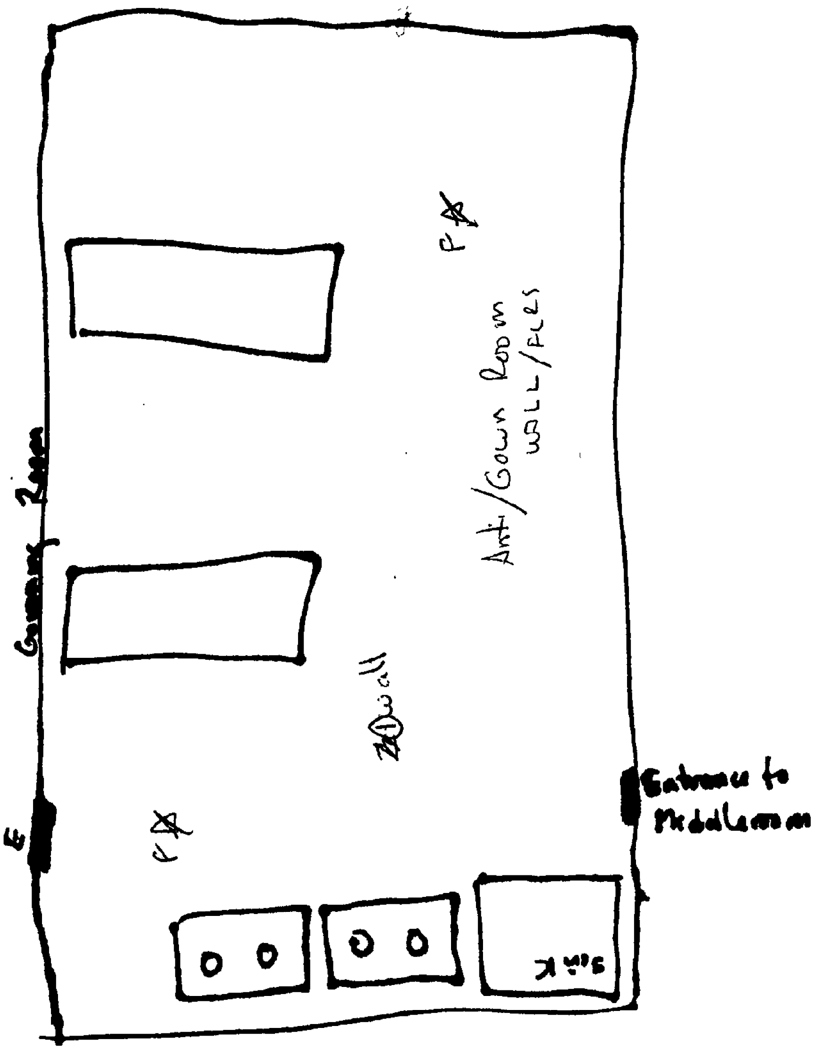
☐ Checklist needs to be Written/Changes are Required → TC change #

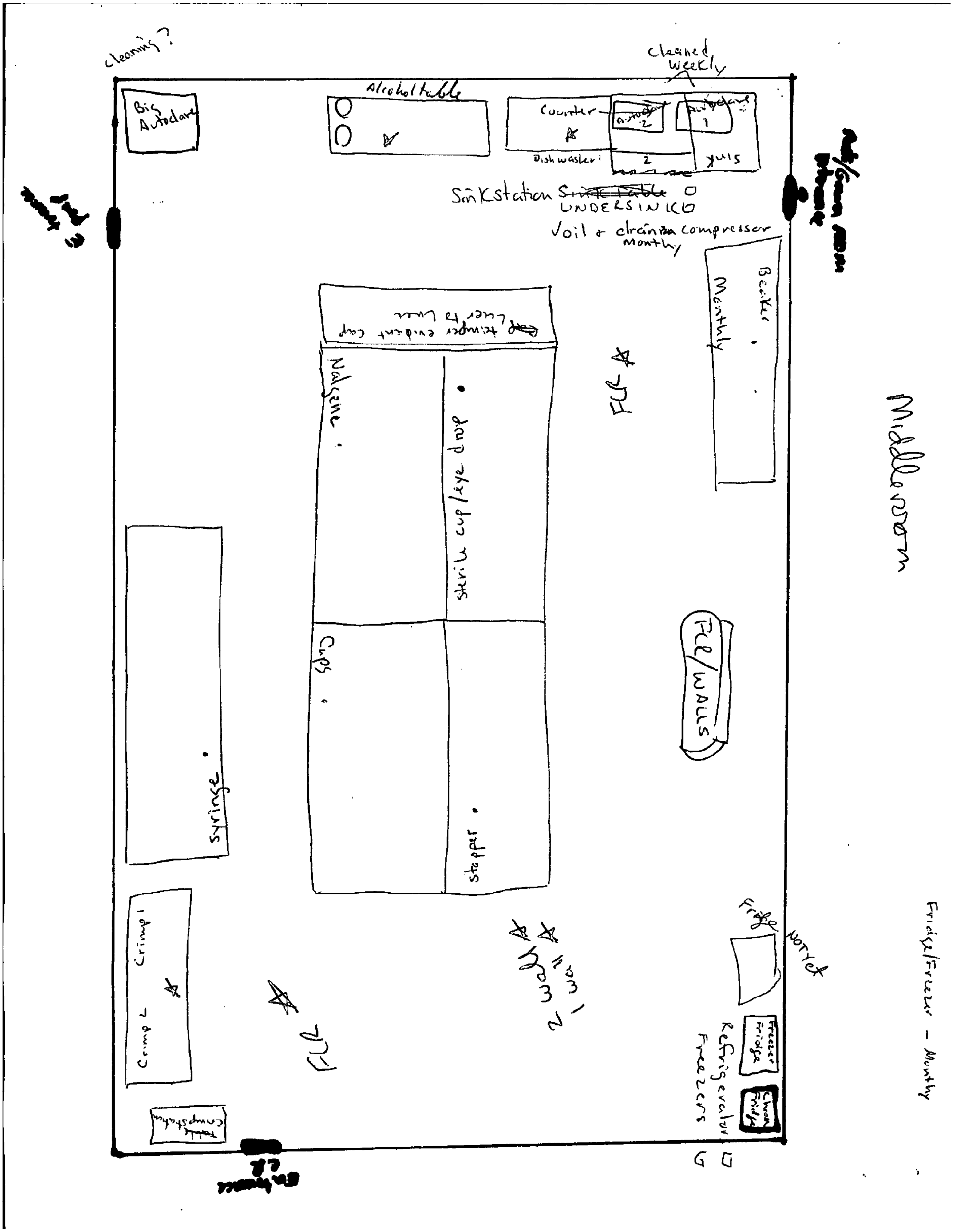
AMR 01-28-09

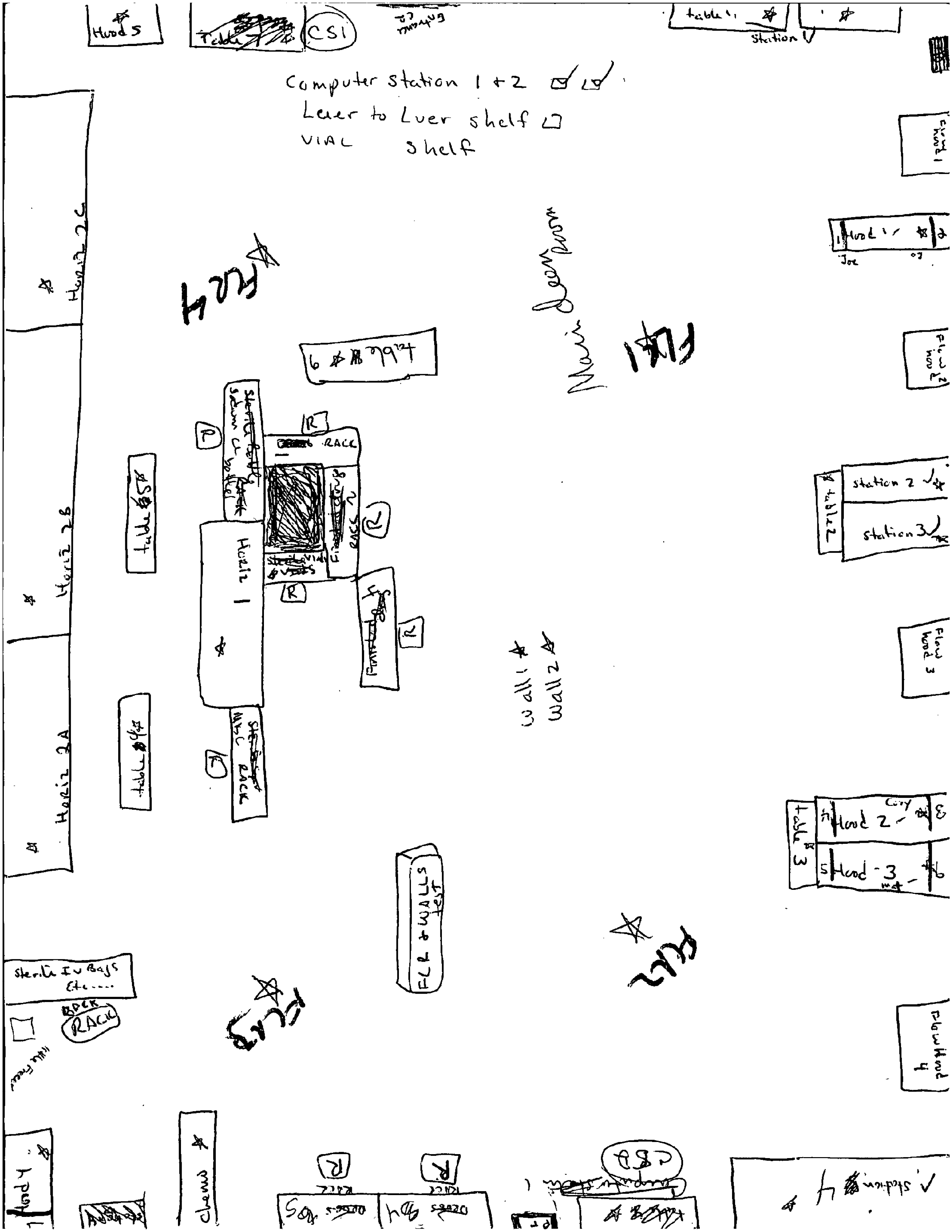
Change Originator:	Printed Name	Signature	Date
Quality Control:	Printed Name	Signature	Date

ORIGINAL

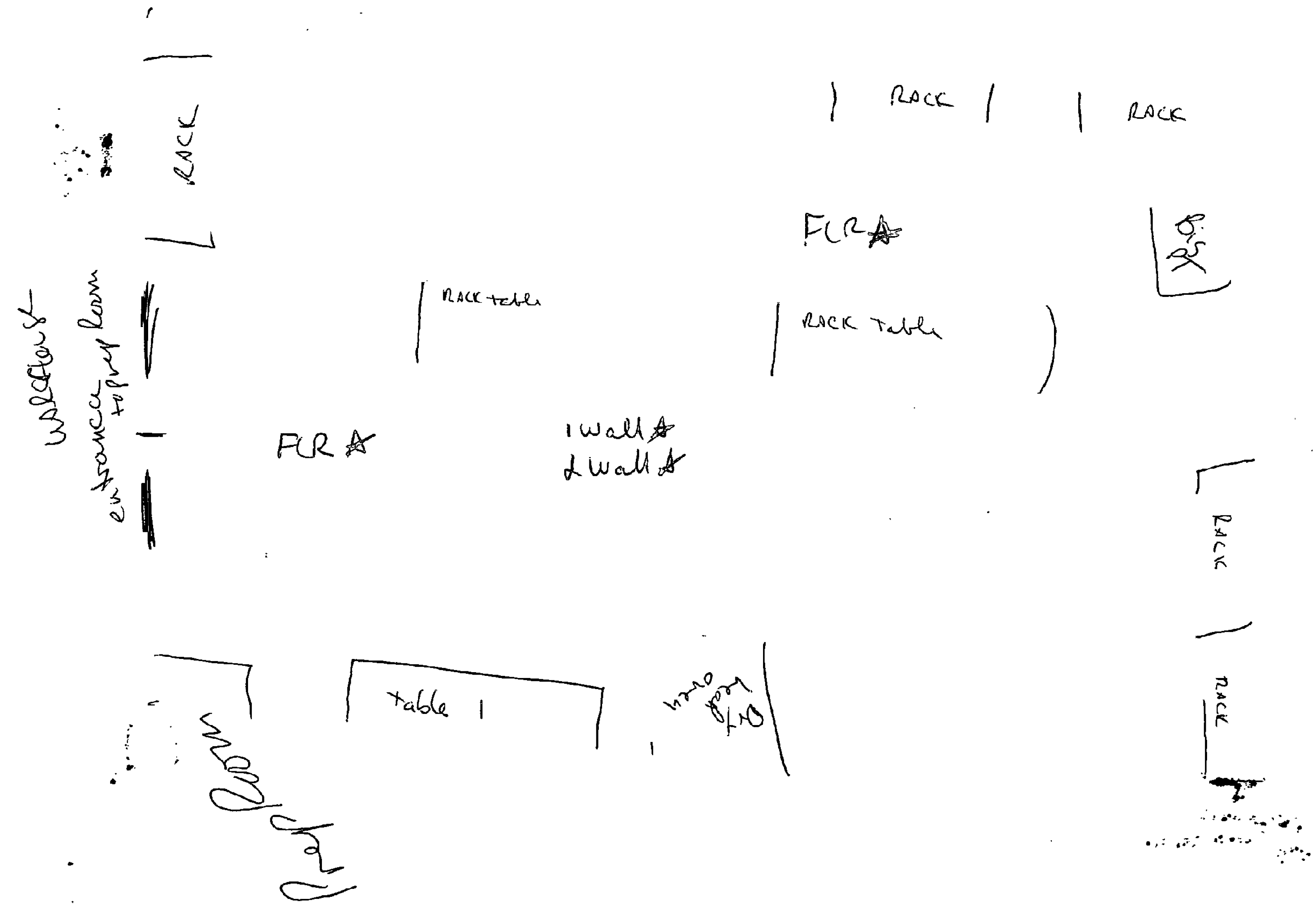
Anti/Gown Room
cleaned weekly




cleaning?
Big Autoclave
Alcohol table
Cleaned weekly
Counter
Autoclave 2
Autoclave 1
Dishwasher 2
sink
Sink station ~~Sink table~~ ☐
UNDERSINK ☐
Void + drain compresser Monthly
[redacted]
[redacted]
Beaker
Monthly
tamper evident cap Luer to Luer
Nalscine
sterile cup/eye drop
Cups
stopper
syringe
FCL
Middleroom
FCL/WALLS
Fridge not yet
Fridge/Freezer - Monthly
2 wall 1 wall
Crimp 1
Crimp 2
FCL
Freezer Fridge
Clean Fridge
Refrigerator Freezers
Table Crimp station
[redacted]
G ☐


Hood 5
Table
CSI
Entrance CR
table 1
Station 1 ✓
Computer station 1 + 2 ☑ ☑
Lever to Luer shelf ☐
VIAL shelf
Flow hood 1
1 Hood 1 ✓ 2
Joe
Horiz 2C
FLR 4
Main clean room
FLR 1
table 6
Flow hood 2
R
RACK
Horiz 2B
table 5
Horiz 1
R
R
R
station 2 ✓
table 2
station 3 ✓
wall 1
wall 2
Flow hood 3
Horiz 2A
table 4
R
RACK
Cory
7 Hood 2 8
table 3
5 Hood 3 6
mat
FLR + WALLS test
FLR 2
FLR 3
Sterile IV Bags Etc....
BACK RACK
Flow hood 4
Hood 4
chems
R
R
CSP
Station 4 ✓

FLRS + WALLS test



SH 1

2

3

4

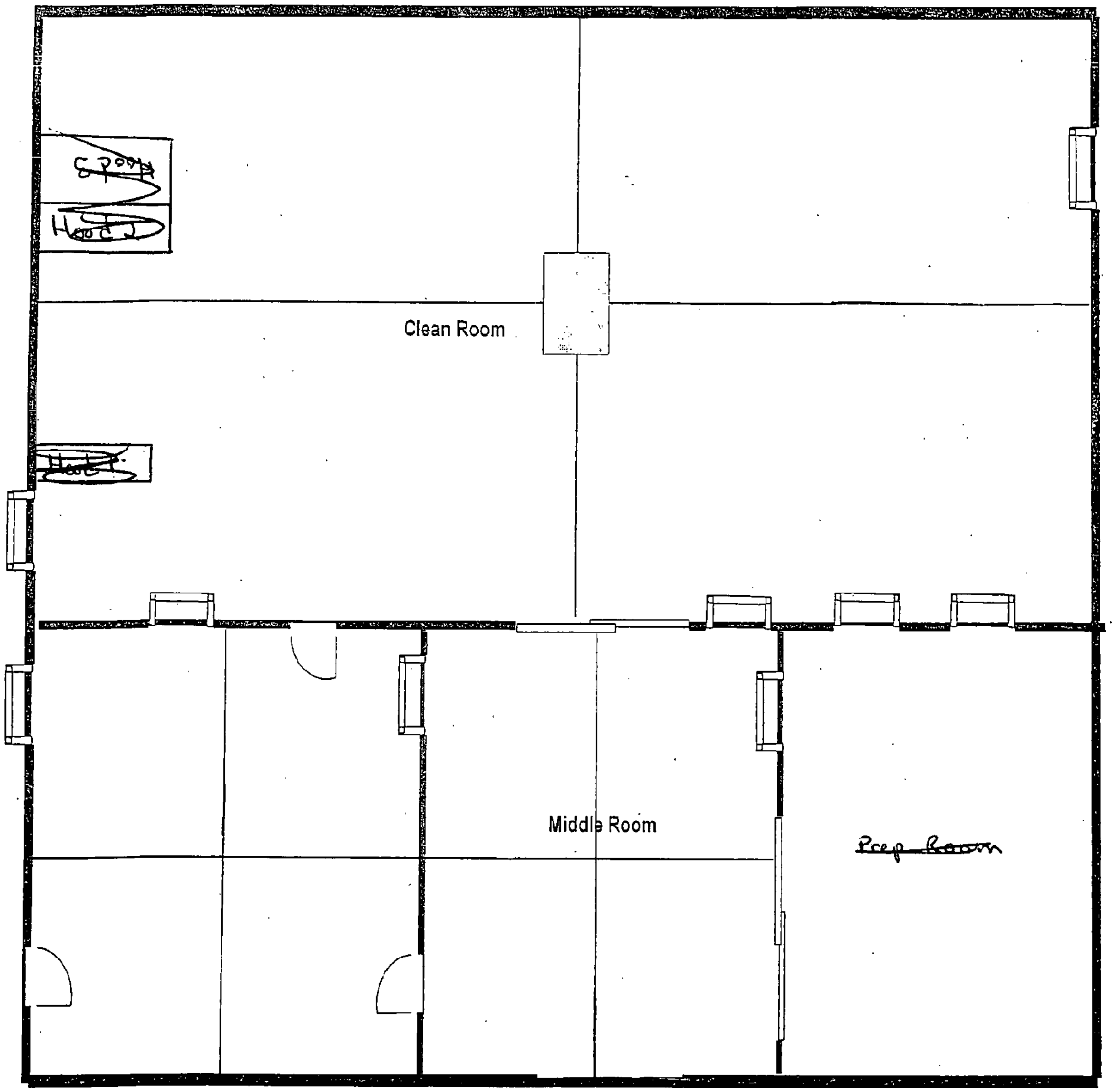
Status Hood

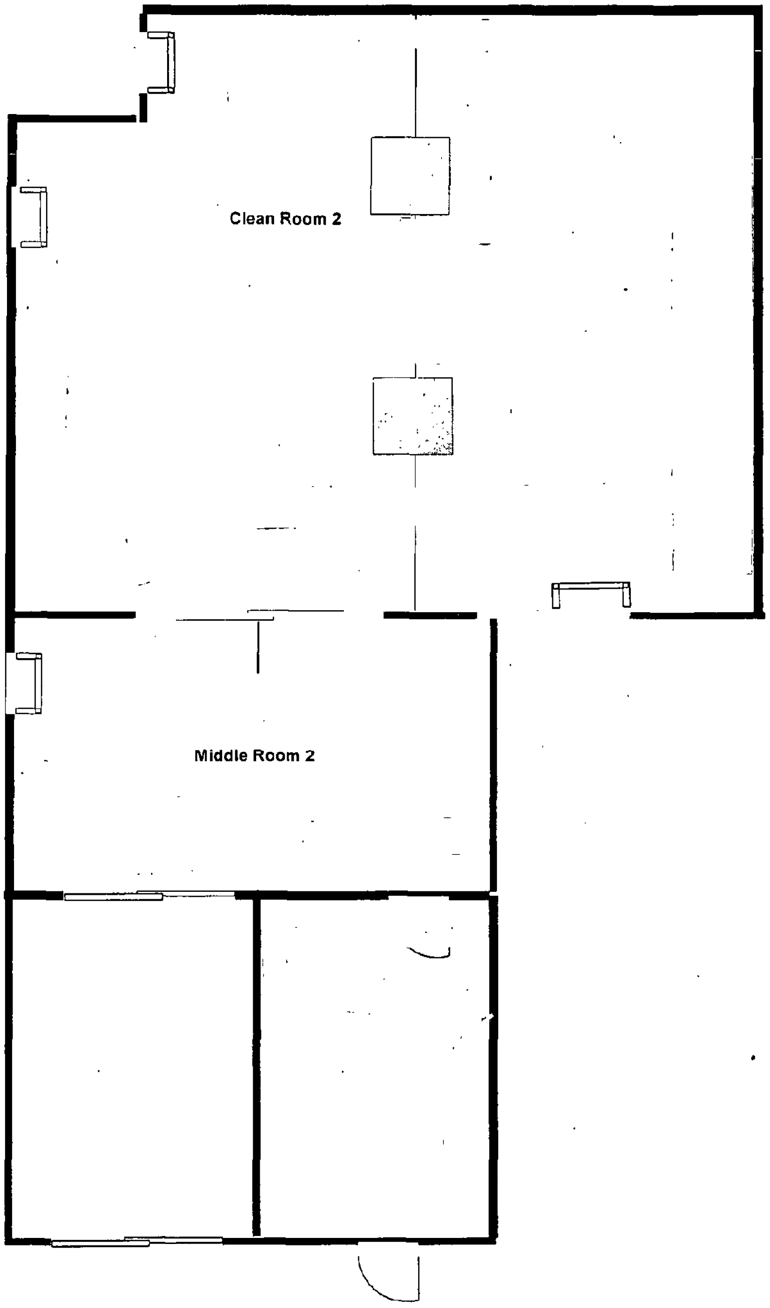
Horiz 1

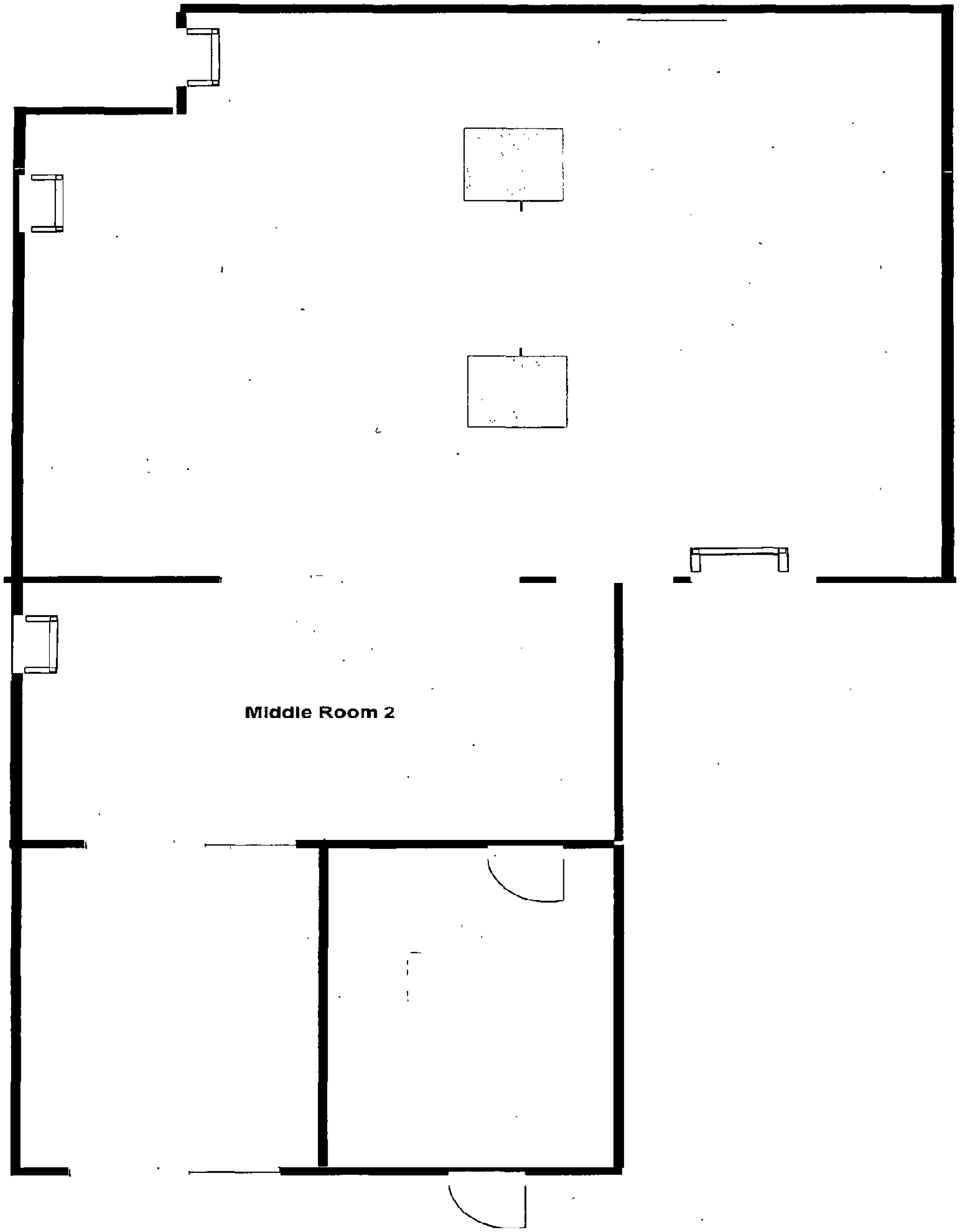
~~Horiz 2~~

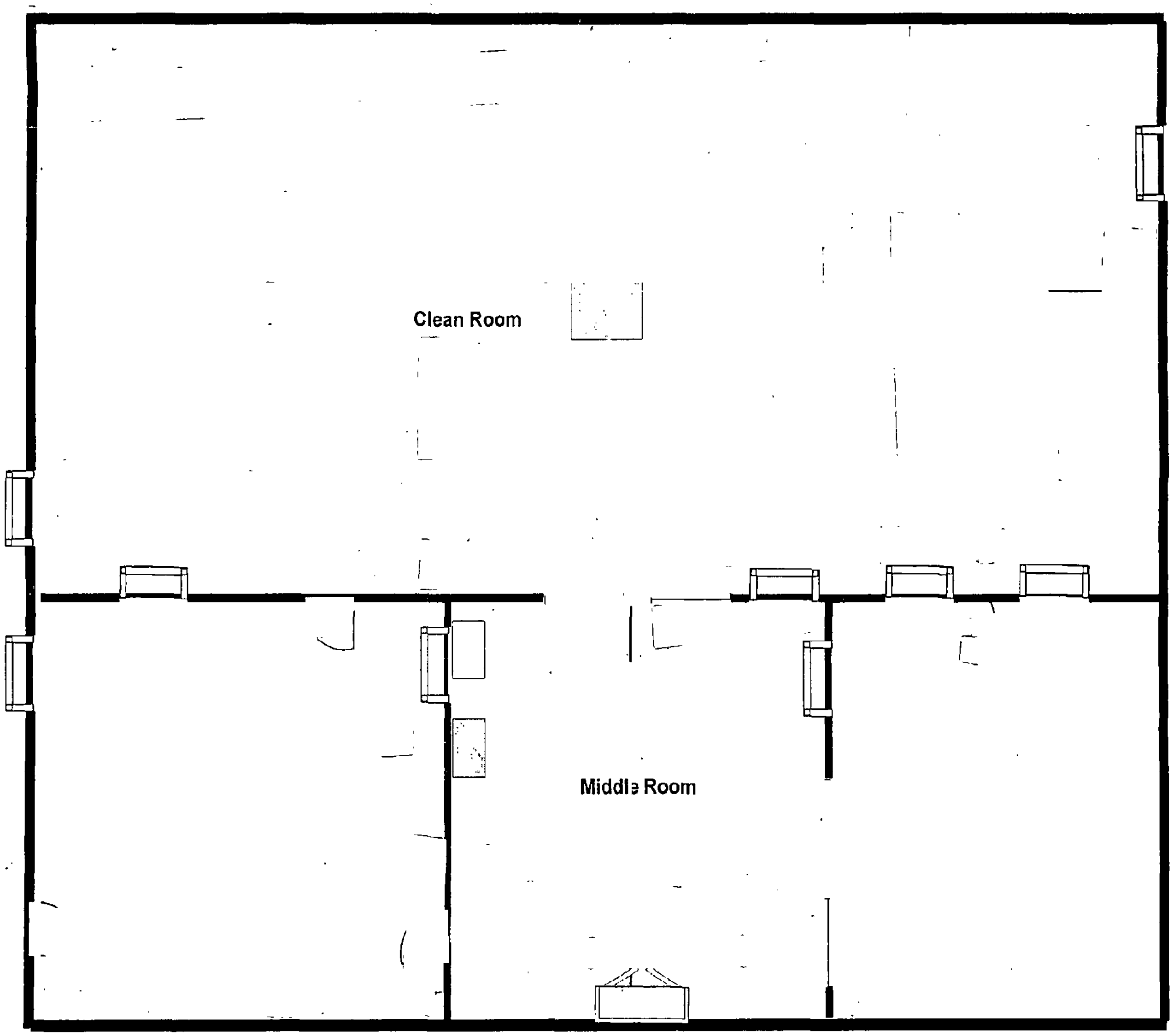
Chemo

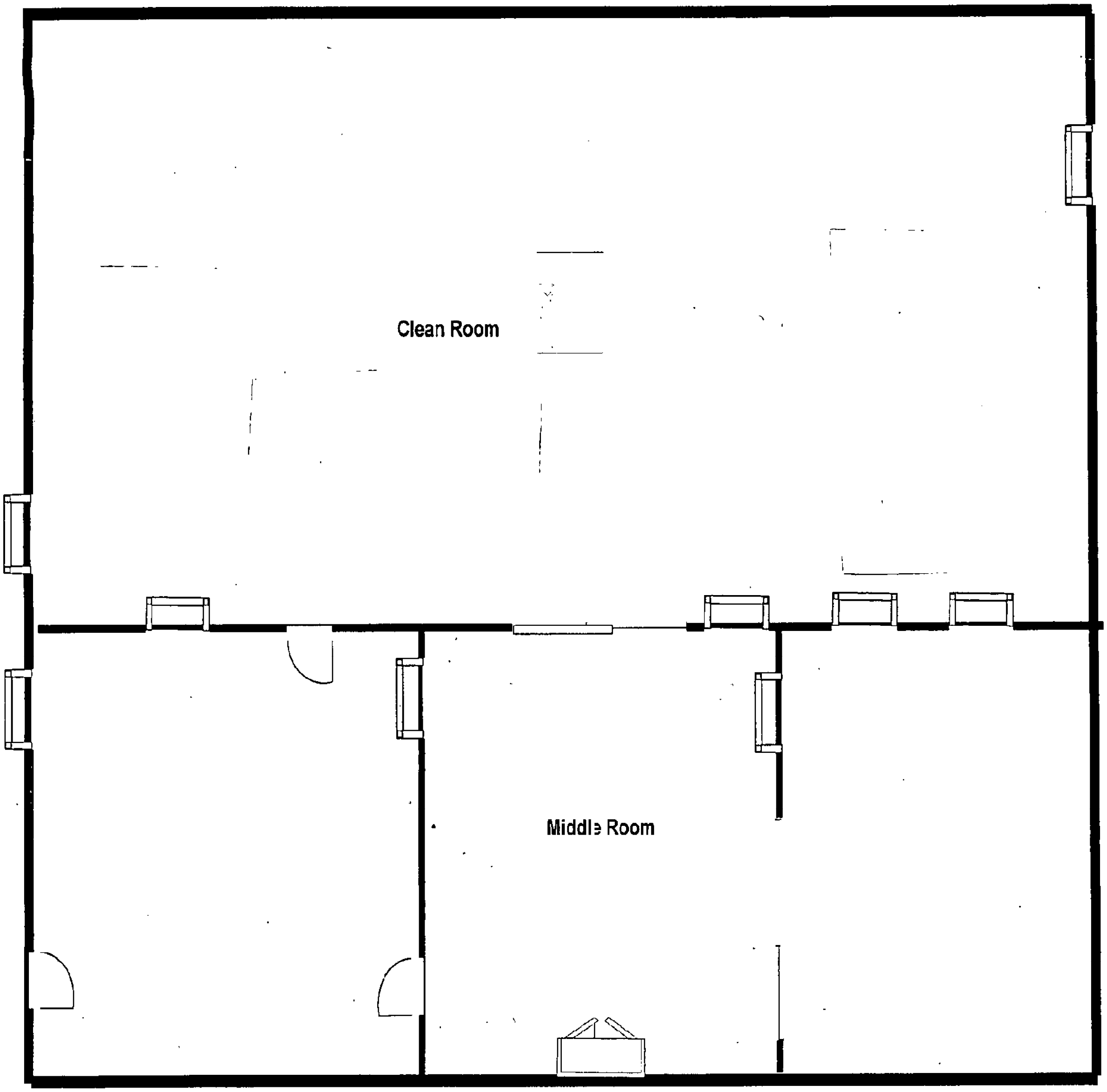
Horiz ~~K~~ 2 ABC


~~Hood 8~~
~~Hood 7~~
Clean Room
Middle Room
~~Prep Room~~

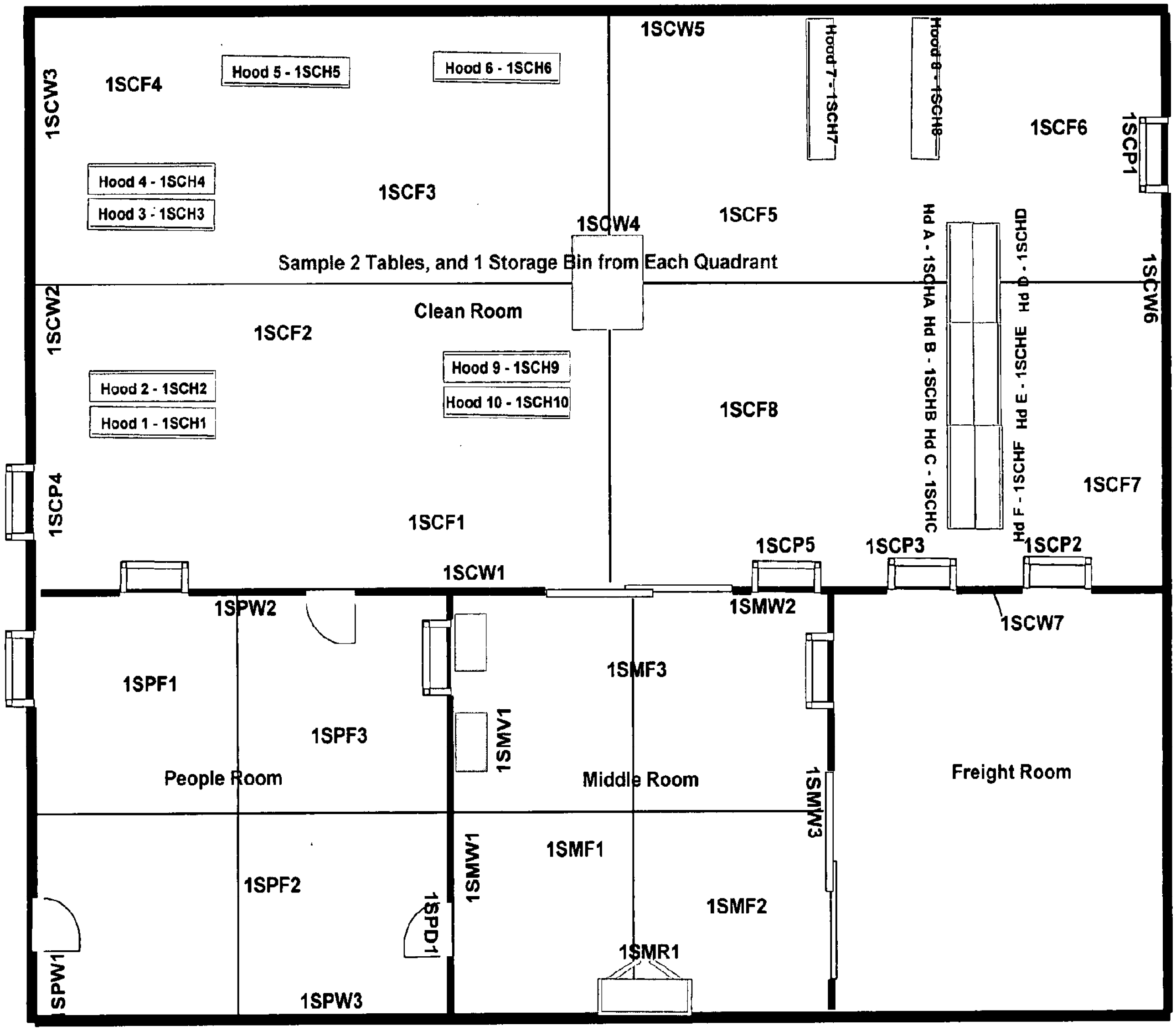

Clean Room 2
Middle Room 2


Middle Room 2

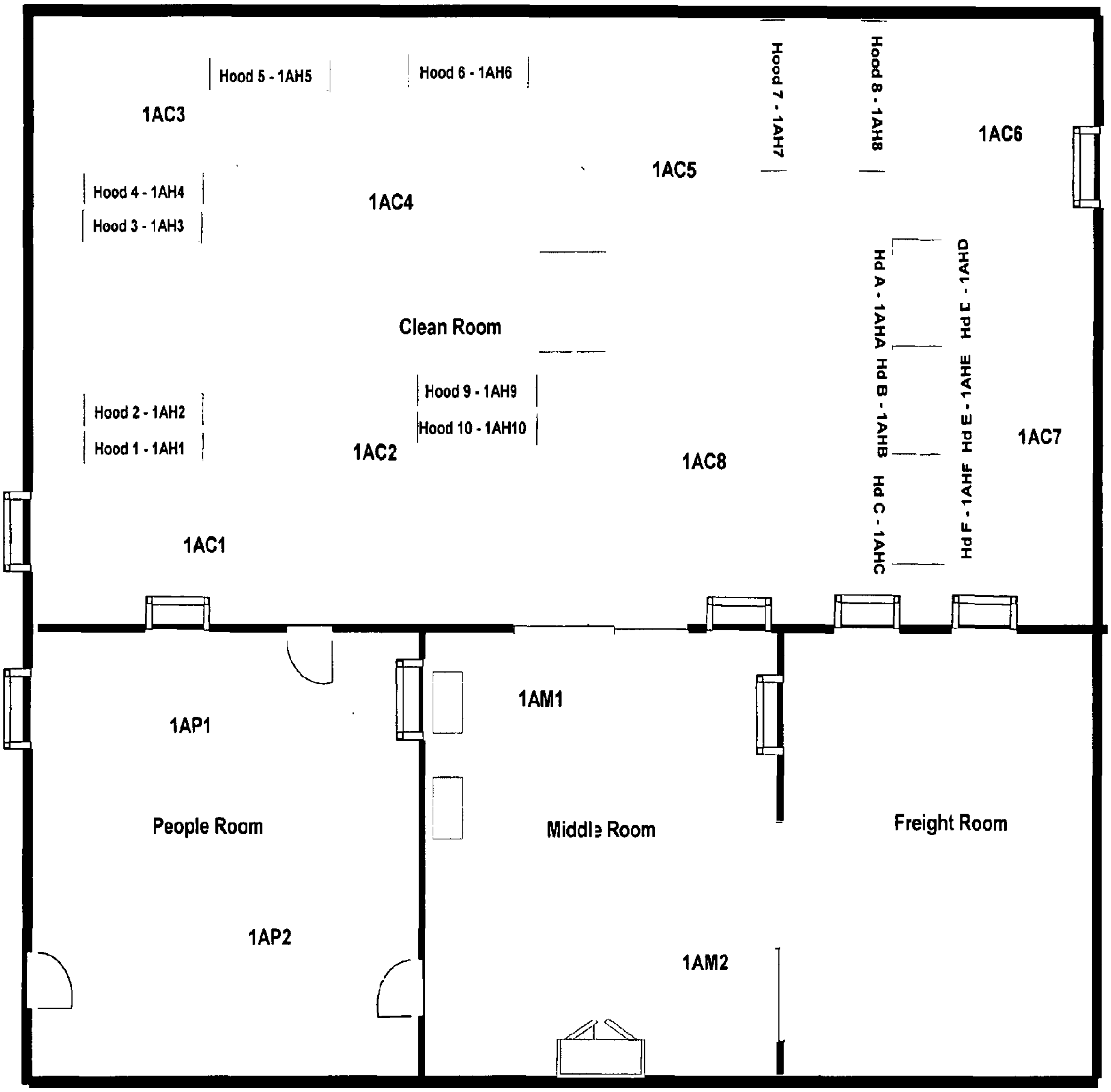

Clean Room
Middle Room

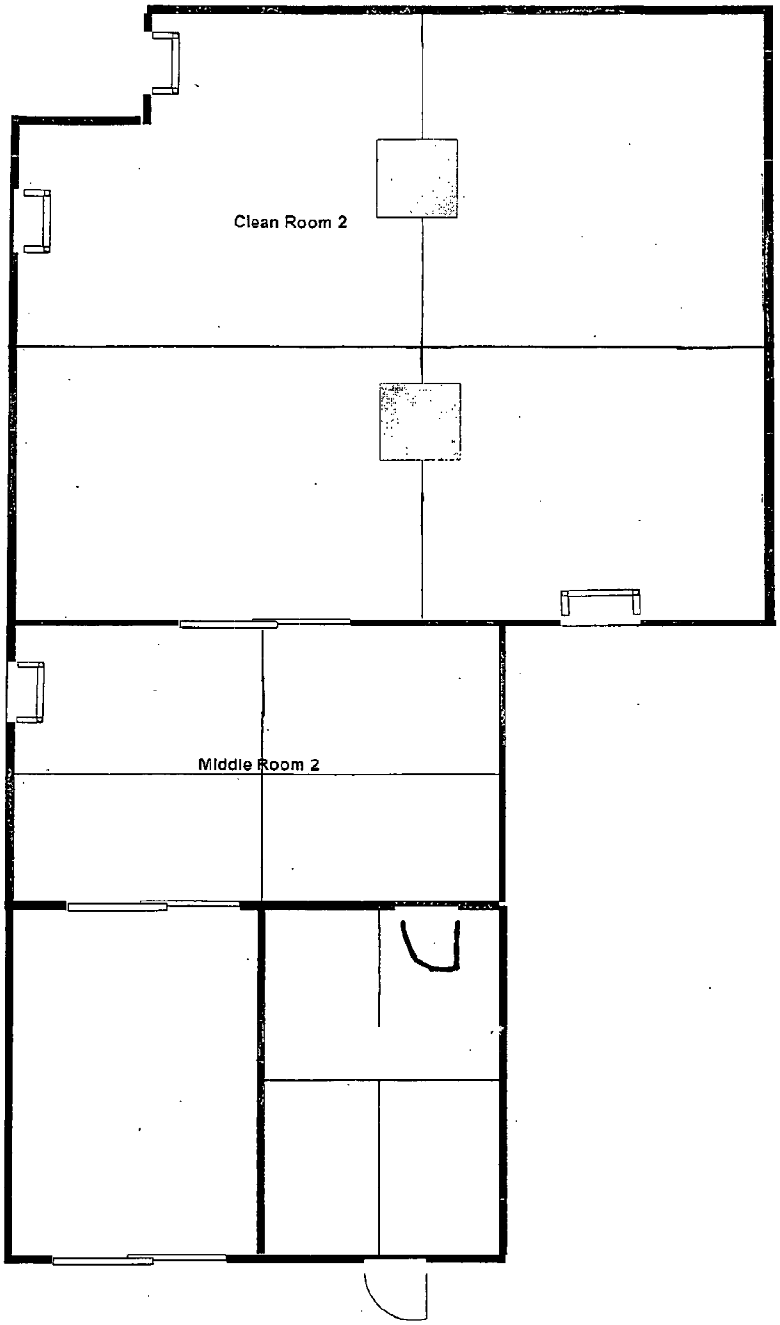

Clean Room
Middle Room

ATTACHMENT 8 – CLEAN ROOM 1 - SURFACE SAMPLING MAP

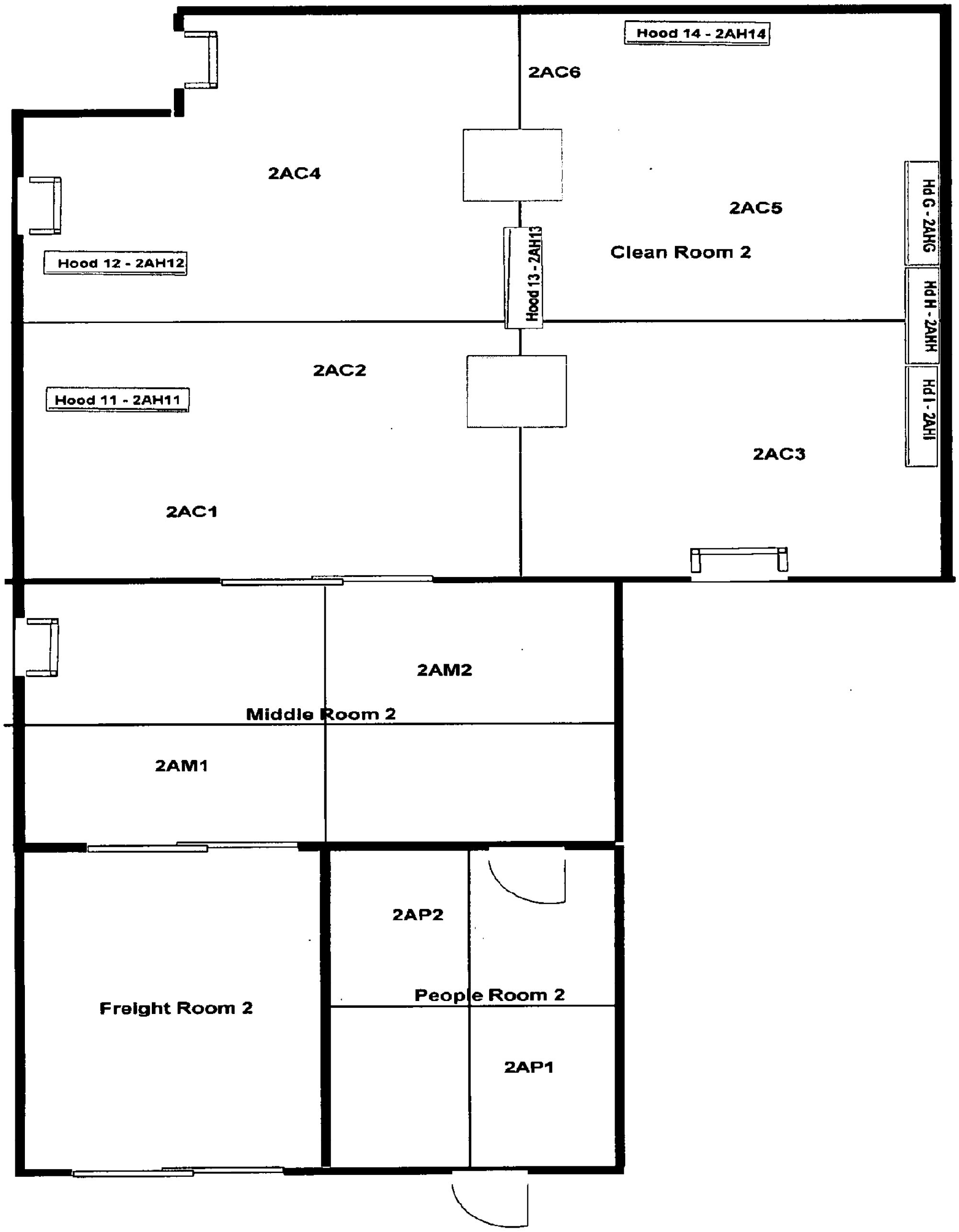


ATTACHMENT 4 – CLEAN ROOM 1 - VIABLE AIR SAMPLING MAP

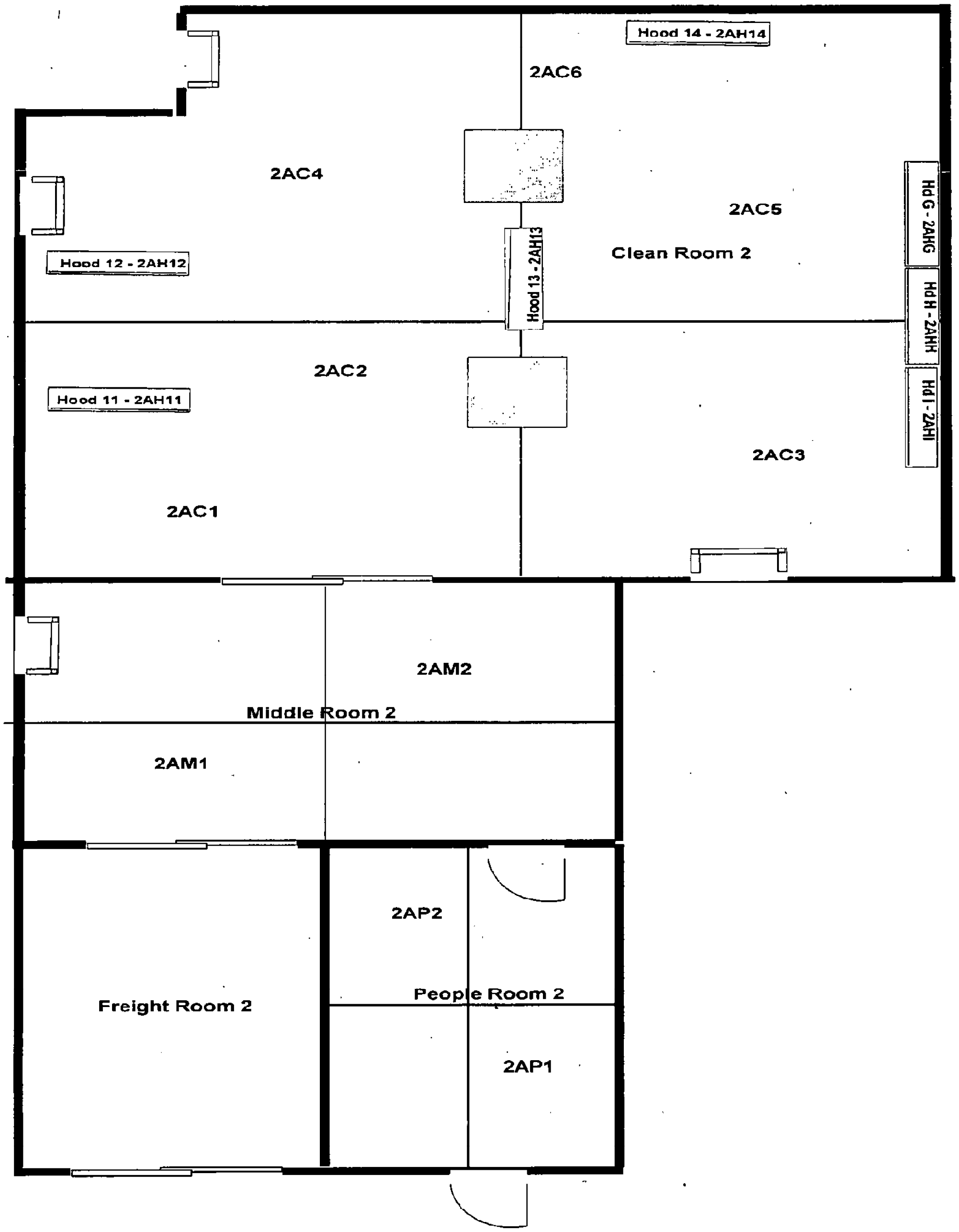



Clean Room 2
Middle Room 2

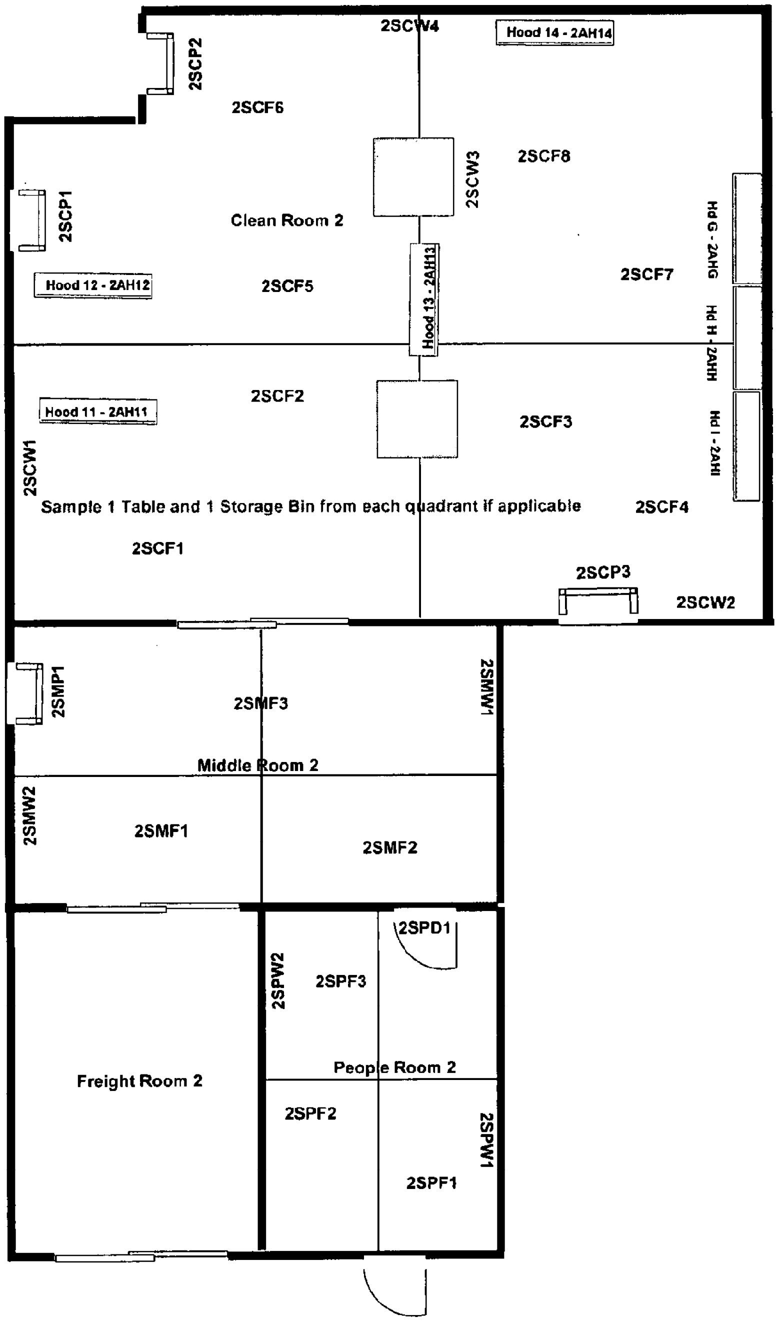
ATTACHMENT 6 – CLEAN ROOM 2 - VIABLE AIR SAMPLING MAP



ATTACHMENT 6 – CLEAN ROOM 2 - VIABLE AIR SAMPLING MAP

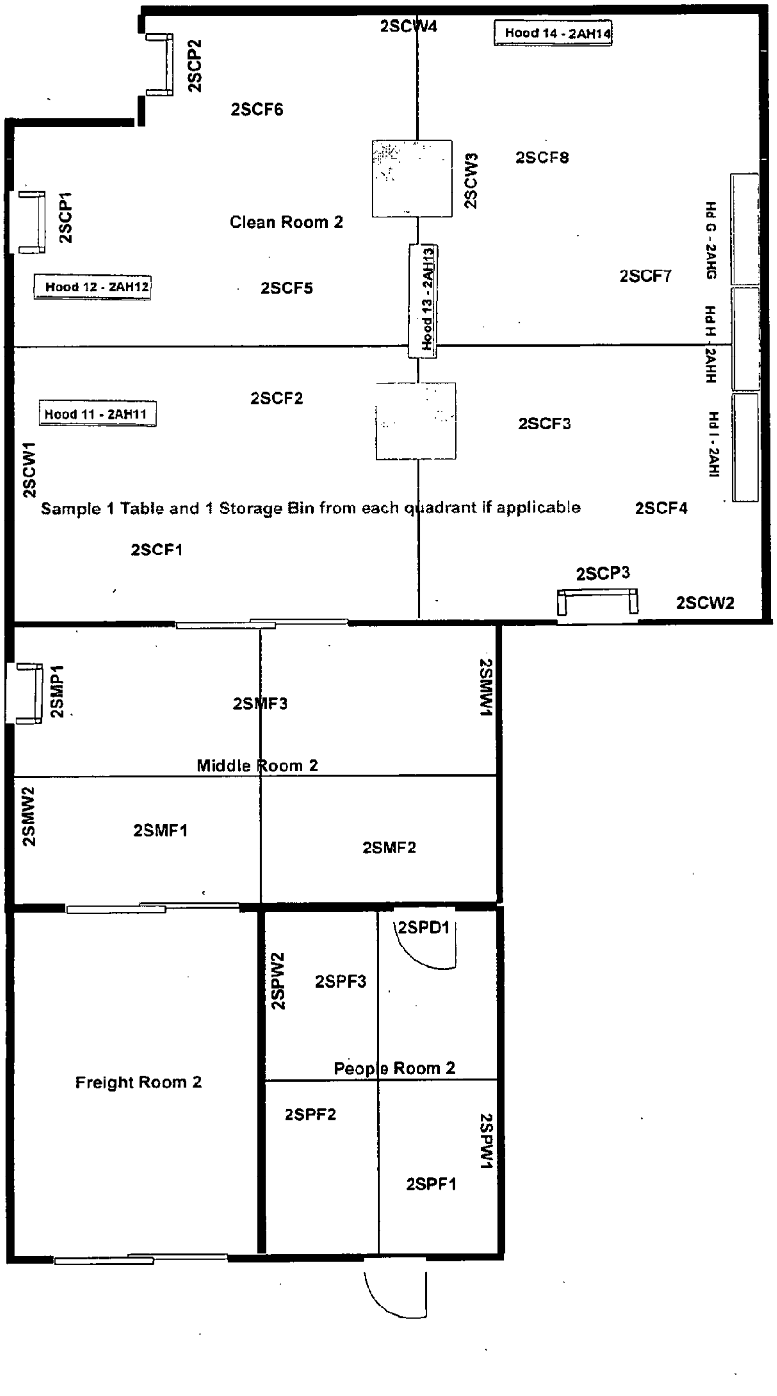


ATTACHMENT 10 – CLEAN ROOM 2 - SURFACE SAMPLING MAP

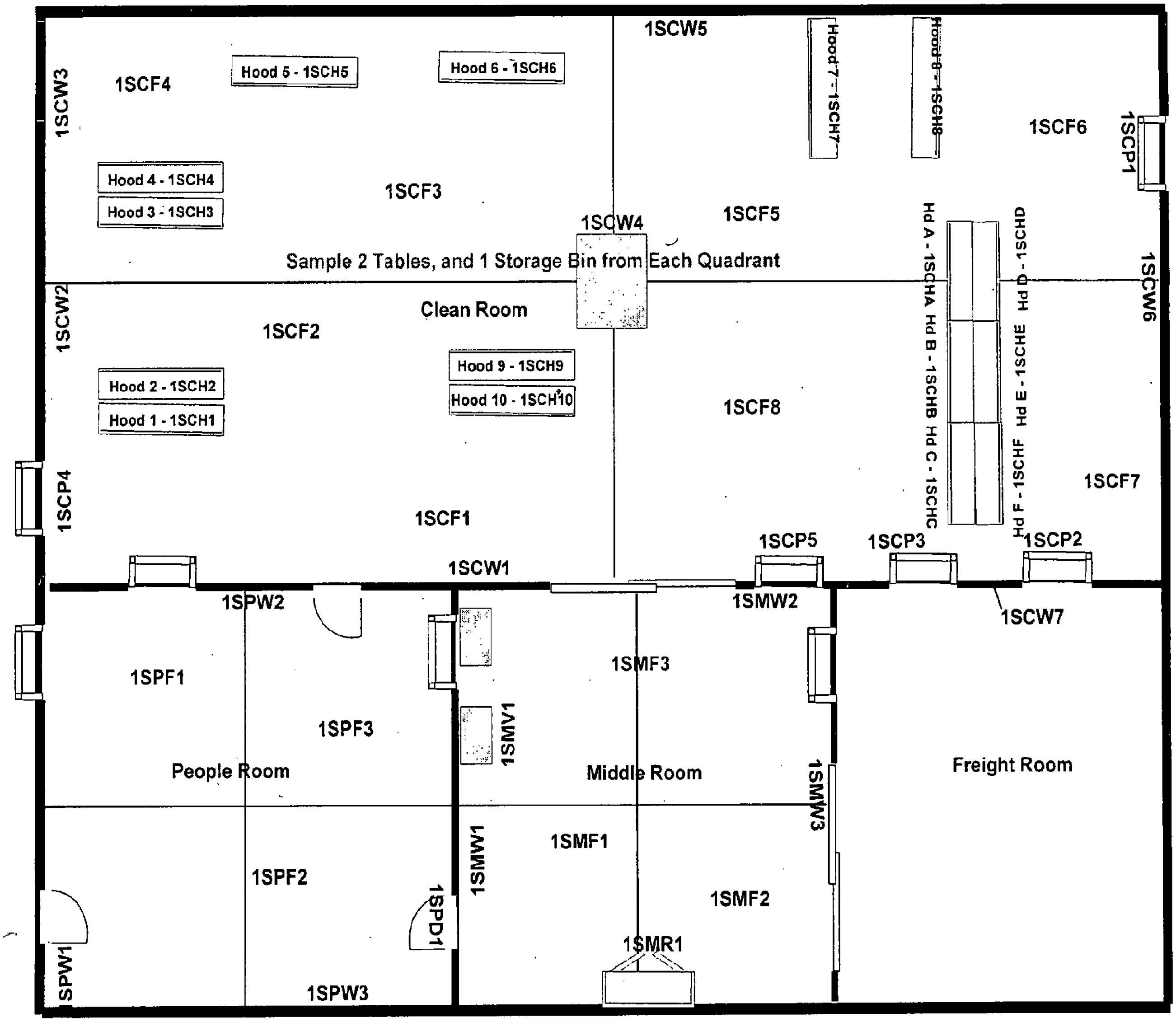


Sample 1 Table and 1 Storage Bin from each quadrant if applicable

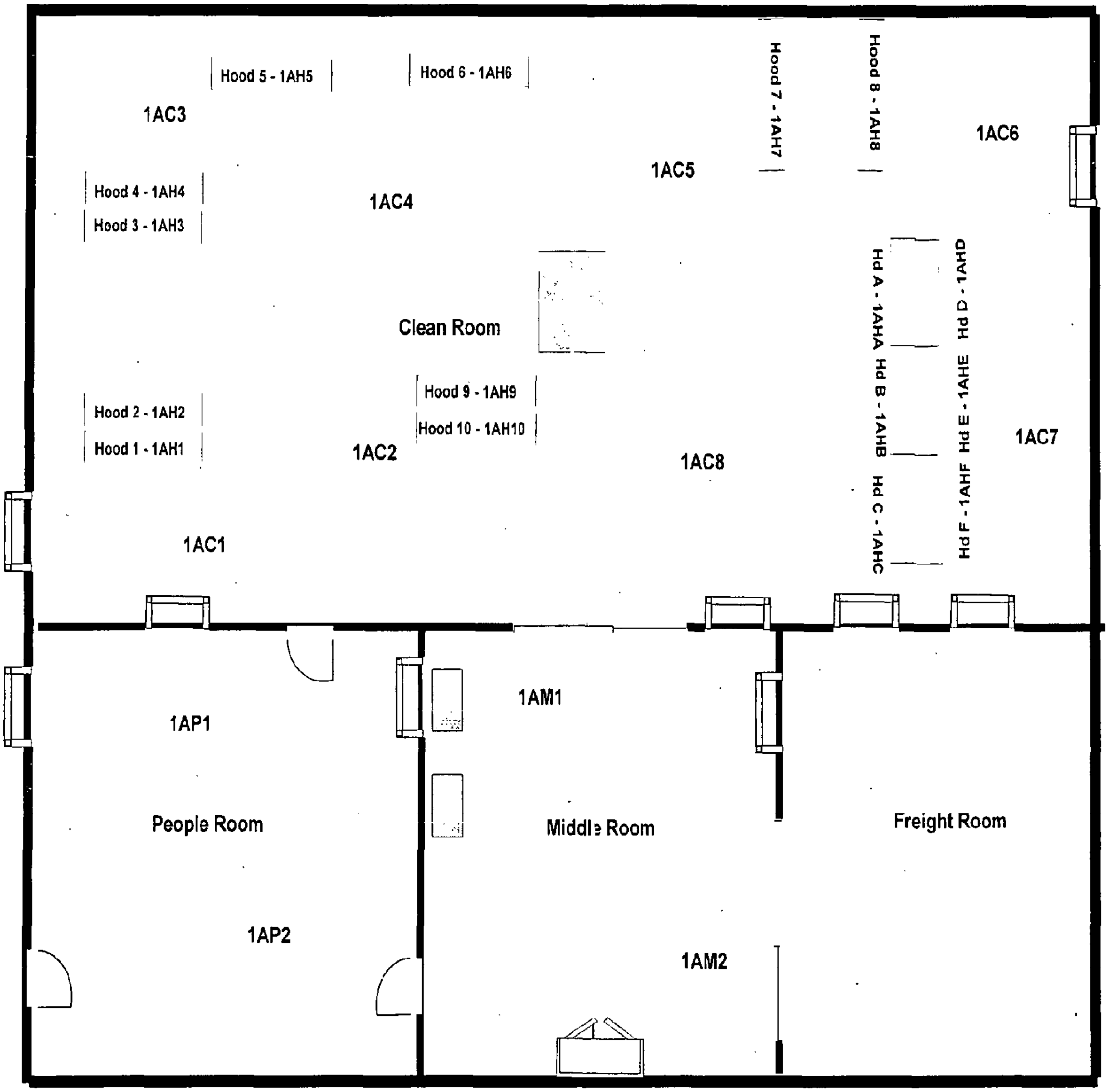
ATTACHMENT 10 – CLEAN ROOM 2 - SURFACE SAMPLING MAP



ATTACHMENT 8 – CLEAN ROOM 1 - SURFACE SAMPLING MAP



ATTACHMENT 4 – CLEAN ROOM 1 - VIABLE AIR SAMPLING MAP



TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 **VERSION NUMBER: 4.0**

Annette ☑

Sterile Laboratory
~~First~~ Effective Date ~~03-28-06~~

Barry III ✓

Originator:
Previous effective Date 11-30-07

Reviewer:
Current Effective Date 09 22 08

OK

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for viable and non-viable environmental monitoring (EM) of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all personnel responsible for EM of the clean room facility comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments"

4.3 ISO 14644-4 "Clean Rooms and Associated Controlled Environments", Part 4

4.4 SOP 3.010 "Sterile Compounding Area Requirements"

4.5 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.6 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 CFU – Colony forming unit

5.2 Viable Particle - A viable particle is a particle that contains one or more living microorganisms.

5.3 Viable Air Sampler - Device used to sample microorganisms in the air.

5.4 Non-Viable Air Sampling - Total particle count. Includes viable particles but does not test for presence of microorganisms.

5.5 Surface Contact Plate - Agar plate used to sample surfaces for microorganisms by direct application. The agar contains neutralizers to inactivate residual disinfectants.

5.6 ISO Classifications

- 5.6.1 ISO Class 4 is equivalent to Class 10 (glove box, antechamber).
- 5.6.2 ISO Class 6 is equivalent to Class 1,000 (main clean room).
- 5.6.3 ISO Class 7 is equivalent to Class 10,000 (gown/crimp room).
- 4.1.1 ISO Class 8 is equivalent to Class 100,000 (prep room).

ORIGINAL
09-22-08

5.7 Alert Level -Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching alert level does not require investigation. (Attachment 6)

5.8 Action Level - Signals a potential drift from normal operating conditions when normal levels of viable particulate in a controlled environment are exceeded; reaching action level requires an investigation and corresponding corrective action. (Attachment 6)

6.0 FREQUENCY

6.1 Personnel touch plates shall be sampled upon completion of sterile compounding and **prior to cleaning**.

6.2 Surface sampling in the glove boxes and antechambers Class 10(ISO Class 4), Class 1000 main clean room(ISO Class 6), Class10,000(ISO Class 7) gown/crimp room, Class100,000(ISO Class 8)prep room, area shall be performed weekly, **prior to cleaning**.

6.3 Sterility of 70% isopropyl alcohol (IPA) will be confirmed weekly. ← Are we still doing this? (BC)

6.4 Viable air sampling shall be performed weekly.

6.5 Non-Viable air sampling shall be performed at least every six months.

6.6 The Pharmacist-in-charge or the Quality Control officer shall review EM data at least every six months to ensure no adverse trends exist.

7.0 EQUIPMENT & SUPPLIES

7.1 Contracted third party (if applicable)

7.2 TSA contact plates containing lecithin and polysorbate 80

7.3 Viable air sampler with sterilized impeller and shroud (Model # SAS180)

7.4 Appropriate user manuals

7.5 Sterile compounding garb

8.0 GENERAL INFORMATION

8.1 EM should flow from "clean" areas to "dirty" areas.

9.0 PROCEDURE

9.1 Upon receipt of commercially prepared TSA contact plates, retain the manufacturer's Certificate of Analysis (CofA). Document receipt of the media on Receipt of Contact plates (Attachment 1).

9.2 Verify that the (CofA) documents the manufacturer's testing of growth promotion. If documentation is not provided, quarantine the media and do not use until appropriate certification is received.

    9.2.1 Remove two plates from new lot of media received for positive and negative controls.

    9.2.2 Label one plate "Positive" and the other plate "Negative," and write the date on each plate.

    9.2.3 Do not expose the agar surface of the "Negative" plate. Seal the contact plate with parafilm.

    9.2.4 For the "Positive" control expose the agar to air for 15 minutes. Seal the contact plate with parafilm.

    9.2.5 Incubate for 5 days at 30°C-35°C. Document on Attachment 1.

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04-22-08

9.2.6 If the positive control has no growth or the negative control has growth, the lot must be rejected.

9.2.7 Place the completed Attachment 1, along with the (CofA) in a designated binder.

9.2.8 Store all acceptable media according to the manufacturer's recommendation in a monitored refrigerator. (2°C - 8°C).

9.3 Viable Air Sampling

9.3.1 Set up the air sampler according to the manufacturer's instructions.

9.3.2 Sanitize the exterior of the air sampler prior to use with a low-lint wipe, saturated with sterile 70% IPA.

9.3.3 If the sampler is being moved from a dirty to clean location during sampling, repeat exterior sanitization.

9.3.4 Make sure the air sampler is programmed with the following parameters:

Sample Time	**Air Volume/Minute**	**Total Air Volume**
5.5 Minutes	180 Liters	1000 liters (35ft^3)

9.3.5 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access." Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.3.6 Document all data on the appropriate Attachments.

9.3.7 Obtain the appropriate quantity of media from storage.

9.3.7.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.3.7.2 Verify media is within expiration date and record media lot number and expiration date on Attachment 4.

9.3.7.3 Aseptically remove an agar contact plate from its package. Make sure that the contact plate covers remains on.

9.3.7.4 Aseptically remove the outer protective cap from the sampler and unscrew the aspirating head.

9.3.7.5 Secure the plate between the metal prongs. Once secure, remove the contact plate cover and immediately replace the aspirating head and screw on tightly.

NOTE: *Do not touch the agar surface (If agar is touched, discard the contact plate).*

9.3.8 Place the air sampler in the desired location at cart or bench top height. Orient the air sampler in a vertical position facing the ceiling and turn on.
Do not place arms over sampler while in operation.

9.3.8.1 The air sampler will automatically turn off at the conclusion of the sampling period.

9.3.8.2 Aseptically remove the contact plate from the sampler. Replace the lid of the contact plate.

9.3.8.2.1 Inspect the contact plate to ensure the impingement marks are present.

9.3.8.2.2 If impingement marks are not present, the sample is invalid and shall be repeated with a new contact plate.

9.3.8.3 Seal the contact plate with parafilm.

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9.3.8.4 Record the site location on the base of the base of the plate, initial and date. Do not record any information on the cover plate.

9.3.8.5 Invert the samples and incubate for as follows.

9.3.8.6 5 days at 30-35 °C.

NOTE: If 5th day of incubation falls on a non-business day, then the plates shall be incubated at that temperature for the remainder of the 7 days. Do not exceed 7 days of incubation.

NOTE: Samples may be shipped to a contract lab for incubation and analysis.

9.4 Non-Viable Air Sampling

9.4.1 Non-viable air sampling shall be performed every 6 months along with Room/Hood Certification.

9.4.2 Sampling shall be performed by an approved vendor using calibrated equipment.

9.4.3 File all completed documents in the designated binder.

9.5 Surface Sampling

9.5.1 Document all data on the appropriate Attachments.

9.5.2 Surface sampling in the glove boxes and antechambers - Class 10 (ISO 4), Class 1000 (ISO 6)main clean room, Class 10,000 (ISO 7)gown/crimp room, Class 100,000 (ISO 8) prep room area shall be performed weekly, **prior to cleaning**

9.5.3 Obtain the appropriate quantity of contact plates from storage.

9.5.3.1 Inspect each plate and discard any damaged or contaminated media and replace.

9.5.3.2 Verify media is within expiration date and record media lot number and expiration date on appropriate Attachment.

9.5.4 Don all appropriate clean room garb and gloves as per SOP 9.090, "Required Garb for Clean Room Facility Access". Be sure to periodically sanitize gloves with sterile 70% IPA while sampling.

9.5.5 Sampling technique:

9.5.5.1 Aseptically remove the contact plate cover and hold the contact plate face down. Gently touch the agar to the desired surface and roll the plate slightly to ensure complete contact with the surface for 10 seconds.

9.5.5.2 Replace the cover and seal the plate with parafilm.

9.5.5.3 Record the site location on the base of the plate. Do not record any information on the cover of the plate.

9.5.5.4 Clean the sample site with sterile 70% IPA before proceeding to the next site.

9.5.6 Incubate for 5 days 30°C-35°C.

9.5.7 Record surface sampling results on Attachment 2, and file all completed documents in the EM binder.

9.6 Confirm the Sterility of 70% IPA

9.6.1 Refer to the appropriate Attachment for Surface Sampling Log

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9.6.2 Obtain two contact plates from storage and test two random sterile 70% IPA bottles.

  9.6.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

  9.6.2.2 Verify media is within expiration date, and record media lot number and expiration date on Attachment 2.

9.6.3 Aseptically remove the contact plate cover.

NOTE: *Do not touch the agar surface (If agar is touched, discard the contact plate).*

9.6.4 Spray the surface of the agar with the sterile 70% IPA designated for use in the clean room.

9.6.5 Replace the cover and seal the plate with parafilm.

9.6.6 Label the base of the plate with "IPA" and the IPA lot number/expiration date. Do not record any information on the cover of the plate.

9.6.7 Incubate for 5 days at 30°C-35°C.

9.6.8 Record results on Attachment 2, and file all completed documents in the EM binder.

9.7 Personnel Monitoring

9.7.1 Refer to the Clean Room Facility Personnel Touch Plate Log (Attachment 5).

9.7.2 Obtain the appropriate quantity of contact plates from storage.

  9.7.2.1 Inspect each plate and discard any damaged or contaminated media and replace.

  9.7.2.2 Verify media is within expiration date.

  9.7.2.3 Label the base of the contact plate with the date, the pharmacist/technician initials, the hand sampled and what product is being compounded.

  9.7.2.4 After sterile compounding is completed for the day, and **prior to cleaning**, touch each gloved finger of the dominant hand to the agar surface, making certain not to re-touch areas.

9.7.3 Replace the cover and seal the plate with parafilm.

9.7.4 Incubate for 5 days at 30°C-35°C.

9.7.5 Record personnel monitoring results on Attachment 5 and file all completed documents in the EM binder.

9.8 The Pharmacist-in-charge or the Quality Control Officer shall review EM data at least every six months to ensure no adverse trends exist.

9.9 Alert and Action Limits

9.9.1 Air Sampling (Viable)

9.9.2 Calculate the level of viable airborne particulates as CFU per cubic foot. The volume of air sampled in the Class 10 (ISO 4) area will be 284 liters (10 cubic feet) and all other locations will be 142 liters (5 cubic feet).

  9.9.2.1 The alert/action limits for air sampling should be derived from historical data. *** Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 6).**

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9.9.3 Surface and Personnel Monitoring

9.9.3.1 Calculate the level of surface and personnel particles as CFU per contact plate.

9.9.3.2 The alert/action limits for surface and personnel monitoring should be derived from historical data. * **Until historical data can be determined, follow the guidelines provided by the USP Proposed Levels for Air and Surface Monitoring (Attachment 6).**

9.10 Investigation and Corrective Actions

9.10.1 **There will be no alert/action levels until historical data can be collected to set appropriate levels. Data should be collected for a minimum of one month prior to setting limits. After one year the levels should be re-evaluated to take into account seasonal changes.**

9.10.2 If an alert level is exceeded, corrective action may not be required, but records should demonstrate that a spike in normal levels was recognized.

9.10.3 If alert levels are consistently exceeding the limits (three consecutive samplings), the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.3.1 Review of sanitation procedures

9.10.3.2 Review of sampling technique

9.10.3.3 Review of clean room personnel

9.10.3.4 Inspection of sampling media

9.10.4 If an excursion occurs above an action level, the Pharmacist-in-charge or Quality Control Officer must be notified and investigation and corrective action should occur. This may include, but is not limited to, the following actions:

9.10.4.1 Identification of microbial isolates to determine origin

9.10.4.2 Review of pressure differential information

9.10.4.3 Review of HEPA and clean room certification

9.10.4.4 Review of Logs of Use, Maintenance and Cleaning (LUMACs)

9.10.5 After the corrective action is taken, the area should be re-sampled three consecutive times. If all samples are within limits, approve the corrective action. If any sample fails, additional investigation is required.

9.11 Non-Routine Samples

9.11.1 Non-routine samples that are not listed on the Viable and Surface Sampling Forms may be taken at a desired location.

9.11.2 Take the sample according to the appropriate air or surface sampling procedure above.

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9.11.3 Document the sample location, sampling (air/surface), and results on Attachment 3.

9.11.4 Non-routine samples are investigational and shall not be compared to alert/action values. Do not generate an alert or action as described in 9.10 for non-routine samples.

9.12 Reporting Results

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9.12.1 Remove samples from the incubator. Record stop times on the appropriate attachment.

9.12.2 Count all colonies on the plate and document results for each category below.

- Bacteria
- Mold (Count or indicate presence)
- Total Counts of Bacteria and Mold combined

10.0 ATTACHMENTS

10.1 Attachment 1 - Receipt of Contact Plates

10.2 Attachment 2 - Clean Room Surface Sampling Diagram and Form

10.3 Attachment 3 - Non-Routine Air/Surface Sample Form

10.4 Attachment 4 - Clean Room Viable Air Sampling Diagram and Form

10.5 Attachment 5 - Clean Room Facility Personnel Touch Plate Log

10.6 Attachment 6 - Levels for Air and Surface Monitoring

1.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06012
2.0	04/06/06	Updated section 9.3 and attachment 1 to include positive/negative controls. Updated sample identification labels and schematic maps on attachments 2, 3, 4 and 5.	CR06053
3.0	11/30/07	Taking out TSA Strips, non-viable samples, fixing iso/ classes not correct	CR07018
4.0	09-22-09	Re did attachments for new clean room, Minor changes	CR08017

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TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY
SOP NUMBER: 3.030 **VERSION NUMBER:** 4.0

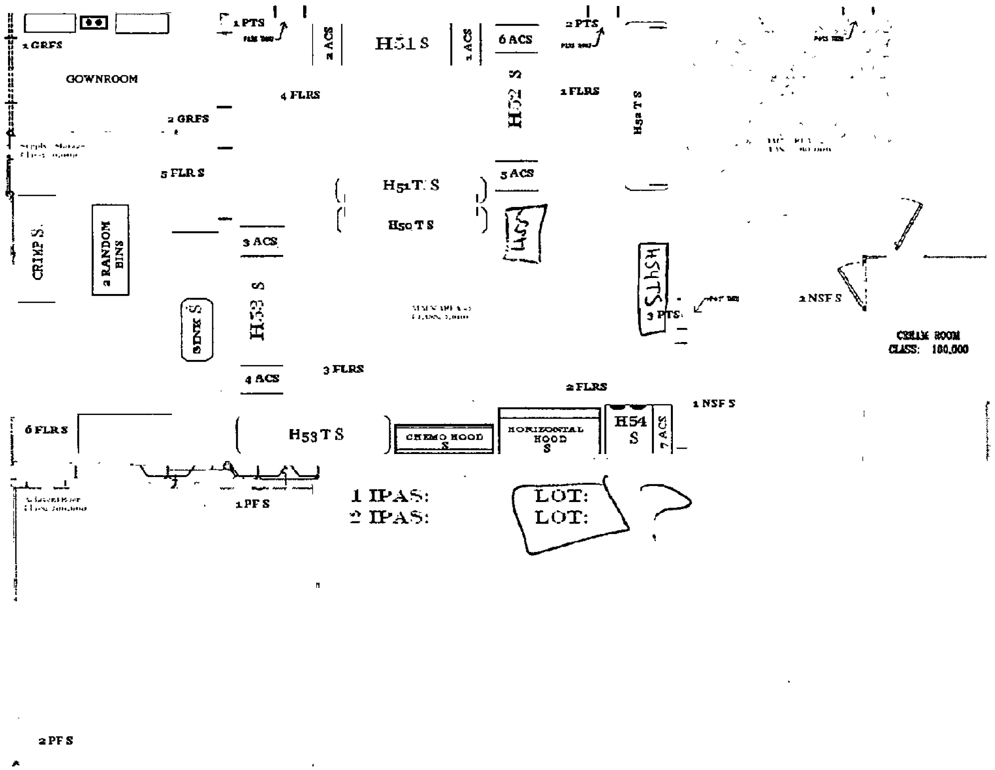
RECEIPT OF CONTACT PLATES - ATTACHMENT 1

Quantity Rec'd (i.e. boxes of 50 plates)	*Manufacturer*	*Lot Number*	*Expiration Date*	*Received By (Initials/Date)*	*Incubation Dates of Positive and Negative Controls 30°C-35°C*	*Positive Control*	*Negative Control*	*Results (CFU)*
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject
					Incubation for 5 days at 30°C-35°C	☐ Growth	☐ Growth	☐ Accept
					→	☐ No Growth	☐ No Growth	☐ Reject

Quality Control: Date:
Revi wed By: Date:

ORIGINAL
NWK 04-22-08

Clean Room Surface Sampling Diagram



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CLEAN ROOM SURFACE SAMPLING - ATTACHMENT 2

(Page 1 of 2)

Add H55S

Add H54TS ->

Sample Location	Description	Results			Alert/ Action
		Bacteria CFU	Mold CFU	Total CFU	
H51S	Hood 1				☐Al ☐Ac
H52S	Hood 2				☐Al ☐Ac
H53S	Hood 3				☐Al ☐Ac
H54S	Hood 4				☐Al ☐Ac
1ACS	Hood 1 Antechamber (Right Side)				☐Al ☐Ac
2ACS	Hood 1 Antechamber (Left Side)				☐Al ☐Ac
3ACS	Hood 2 Antechamber (Right Side)				☐Al ☐Ac
4ACS	Hood 2 Antechamber (Left Side)				☐Al ☐Ac
5ACS	Hood 3 Antechamber (Left Side)				☐Al ☐Ac
6ACS	Hood 3 Antechamber (Right Side)				☐Al ☐Ac
7ACS	Hood 4 Antechamber				☐Al ☐Ac
ChemoS	Chemo Hood				☐Al ☐Ac
HorizS	Horizontal Hood				☐Al ☐Ac
H50TS	Table 1				☐Al ☐Ac
H51TS	Table 2				☐Al ☐Ac
H52TS	Table 3				☐Al ☐Ac
H53TS	Table 4				☐Al ☐Ac
1PTS	Pass - thru				☐Al ☐Ac
2PTS	Pass - thru				☐Al ☐Ac
3PTS	Pass - thru				☐Al ☐Ac

ORIGINAL 08-22-08

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 VERSION NUMBER: 4.0

Random

Change Sheet

NON-ROUTINE AIR/SURFACE SAMPLE FORM - ATTACHMENT 3

Surface Sample Location	Description	Results Bacteria CFU	Mold CFU	Total CFU

Date of Sampling: Media Lot#: Exp Date:
Date placed in incubator: (Incubate for 5 days at 30-35 °C)
Reason for Sampling:

Air Sample Location	Description	Results Bacteria CFU	Mold CFU	Total CFU

Date of Sampling: Media Lot#: Exp Date:
Sampler Mfg/Model: Calibration Due Date:
Date placed in incubator: (Incubate for 5 days at 30-35 °C)
Reason for Sampling:

Quality Control: Date:
Reviewed By: Date:

ORIGINAL
04-22-08

CLEAN ROOM SURFACE SAMPLING - ATTACHMENT 2

(Page 2 of 2)

Sample Location	Description	Results			Alert/ Action
		Bacteria CFU	Mold CFU	Total CFU	
SinkS	Sink in Crimp Room				☐Al ☐Ac
CrimpS	Crimping Bench				☐Al ☐Ac
1RBS	Random Bin				☐Al ☐Ac
2RBS	Random Bin				☐Al ☐Ac
1GRFS	Gown Room – Near Hall				☐Al ☐Ac
2GRFS	Gown Room – Near Clean room				☐Al ☐Ac
1PFS	Prep Room – Near Incubator				☐Al ☐Ac
2PFS	Prep Room – Near Warehouse				☐Al ☐Ac
1FLRS	Clean Room Floor				☐Al ☐Ac
2FLRS	Clean Room Floor				☐Al ☐Ac
3FLRS	Clean Room Floor				☐Al ☐Ac
4FLRS	Clean Room Floor				☐Al ☐Ac
5FLRS	Clean Room Floor				☐Al ☐Ac
6FLRS	Clean Room Floor				☐Al ☐Ac
1IPAS	Isopropyl Alcohol				☐Al ☐Ac
2IPAS	Isopropyl Alcohol				☐Al ☐Ac

Alert		Action
1 CFU	ISO 4 (class 10) Glove box, Antechambers	2+ CFU
3 CFU	ISO 6 (class 1,000) Main Clean room	5+ CFU
5 CFU	ISO 7 (class 10,000) Gown room, Crimp room	7+ CFU
8 CFU	ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling: Media Lot: Exp Date:

Quality Control: Date:
Reviewed By: Date:

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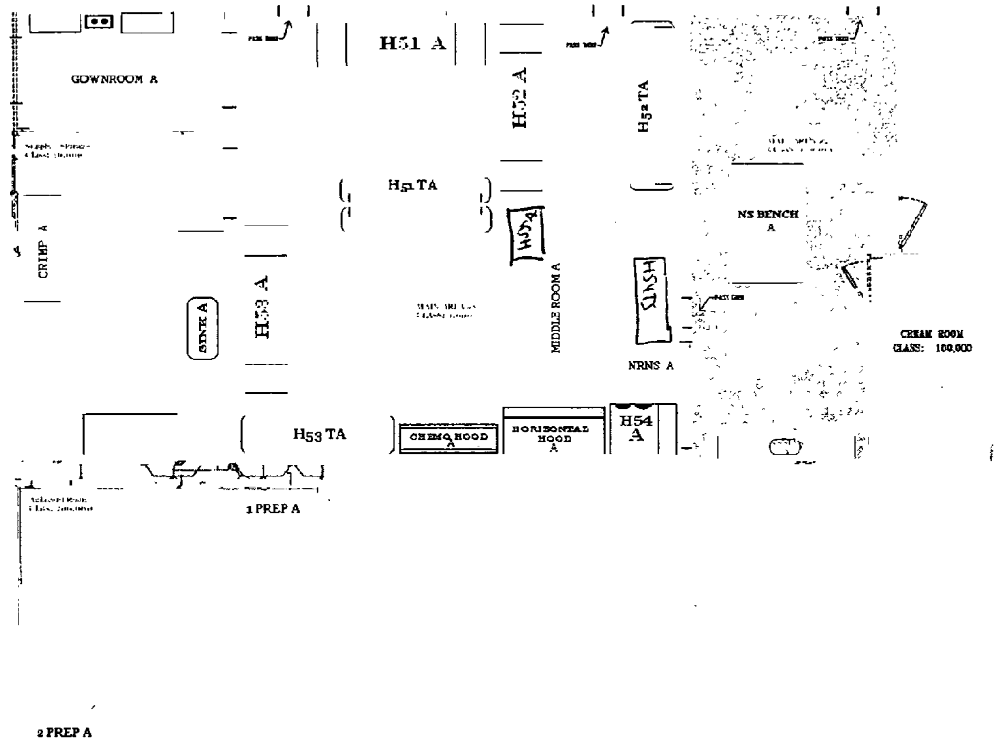
AWK 04-22-08

Clean Room Viable Air Sampling Diagram



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TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY
SOP NUMBER: 3.030 VERSION NUMBER: 4.0

CLEAN ROOM VIABLE AIR SAMPLING - ATTACHMENT 4

Page 1 of 1

→H55X

Sample Location	Description	Results			Alert/Action
		Bacteria CFU	Mold CFU	Total CFU	
H51A	Hood 1				☐Al ☐Ac
H52A	Hood 2				☐Al ☐Ac
H53A	Hood 3				☐Al ☐Ac
H54A	Hood 4				☐Al ☐Ac
ChemoA	Chemo Hood				☐Al ☐Ac
HorizA	Horizontal Hood				☐Al ☐Ac
H51TA	Table 2				☐Al ☐Ac
H52TA	Table 3				☐Al ☐Ac
H53TA	Table 4				☐Al ☐Ac
GownroomA	Gowning Area				☐Al ☐Ac
SinkA	Sink Area				☐Al ☐Ac
CrimpA	Crimping Bench				☐Al ☐Ac
MiddleroomA	Middle of Room				☐Al ☐Ac
NRNSA	Near Non-Sterile Lab				☐Al ☐Ac
1PrepA	Prep Room – Near Incubator				☐Al ☐Ac
2PrepA	Prep Room – Near Warehouse				☐Al ☐Ac

Alert		**Action**
1 CFU	ISO 4 (class 10) Glove box, Antechambers	2+ CFU
2 CFU	ISO 6 (class 1,000) Main Clean room	3+ CFU
5 CFU	ISO 7 (class 10,000) Gown room, Crimp room	8+ CFU
8 CFU	ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling: Media Lot: Exp Date:
Sampler Mfg/Model: Serial #: Calibration Due Date:

Quality Control: Date:
Reviewed By: Date:

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04-22-08

CLEAN ROOM FACILITY PERSONNEL TOUCH PLATE LOG - ATTACHMENT 5

Media Lot # and Exp Date	Rph/Tech	Location and Product Being worked on	Incubation for 5 days at 30ºC - 35ºC	Results (CFU)	Alert / Action
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac
			→		☐ Al ☐ Ac

Alert Level 1+ CFU
Action Level 2+ CFU

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Quality Control: Date:
Revi wed By: Dat :

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 **VERSION NUMBER:** 4.0

LEVELS FOR AIR AND SURFACE MONITORING - ATTACHMENT 6

Note: ** Alert/Action Levels are to be determined after historical data is collected**

Levels for Air Sampling

Classifications	Alert Level	Action Level
ISO 4 (Class 10) Glove box, Antechambers	1 CFU	2+ CFU
ISO 6 (Class 1,000) Main Clean Room	2 CFU	3+ CFU
ISO 7(Class 10,000) Gown room, Crimp Room	5 CFU	8+ CFU
ISO Class 8 (Class 100,000) Prep Room	8 CFU	10+ CFU

Levels for Surface Sampling

Classifications			Alert Level	Action Level
ISO 4 (Class 10) Glove box, Antechambers			1 CFU	2+ CFU
ISO 6 (Class 1,000) Main Clean Room			3 CFU	5+ CFU
ISO 7(Class 10,000) Gown room, Crimp Room			5 CFU	7+ CFU
ISO Class 8 (Class 100,000) Prep Room			8 CFU	10+CFU

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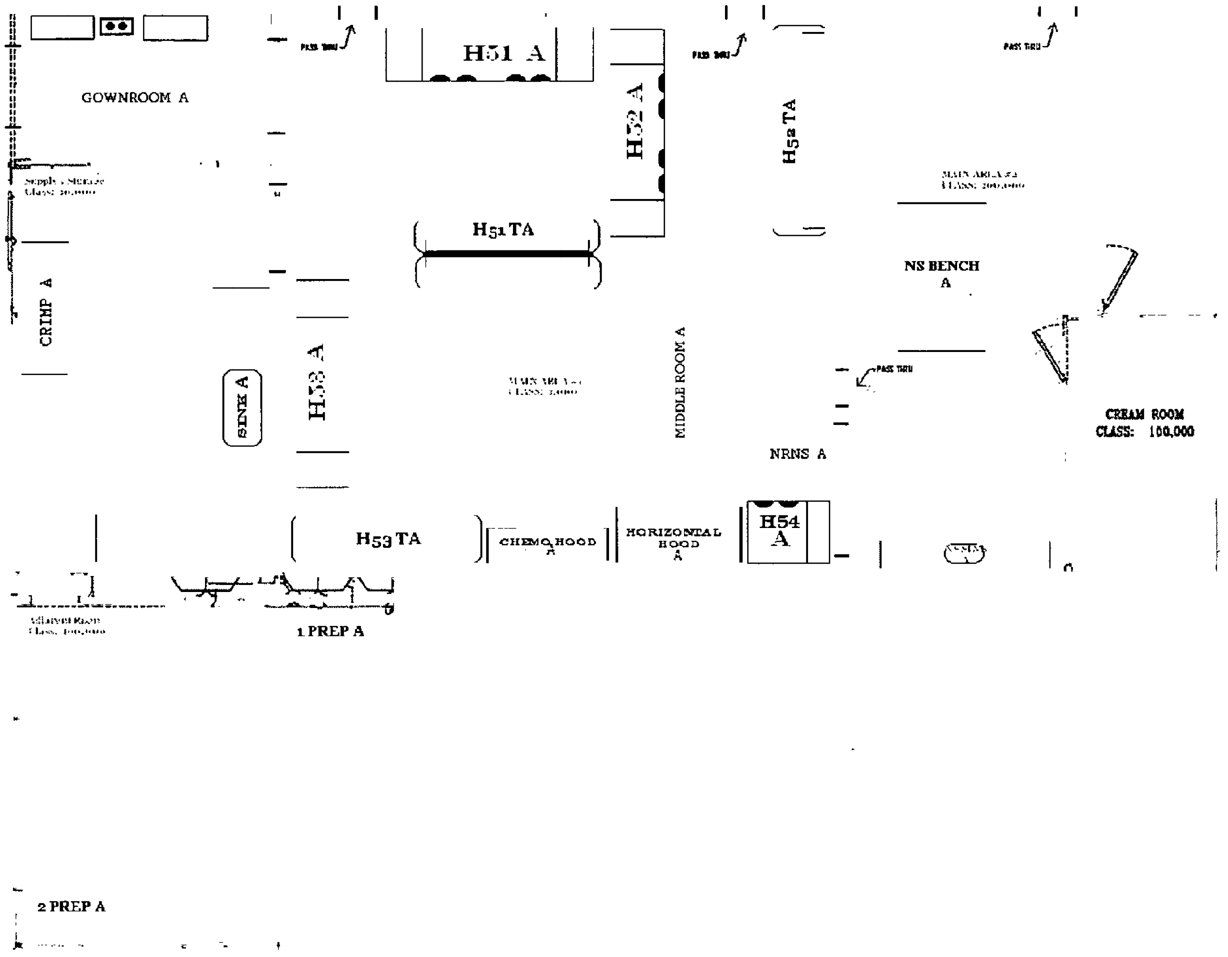
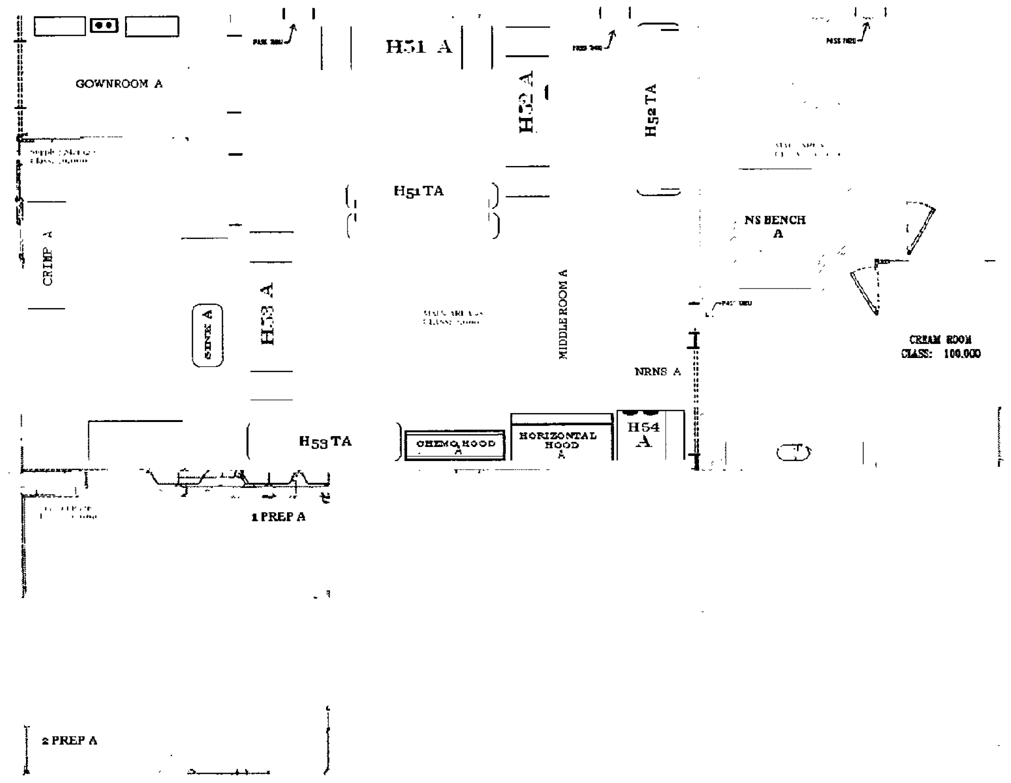
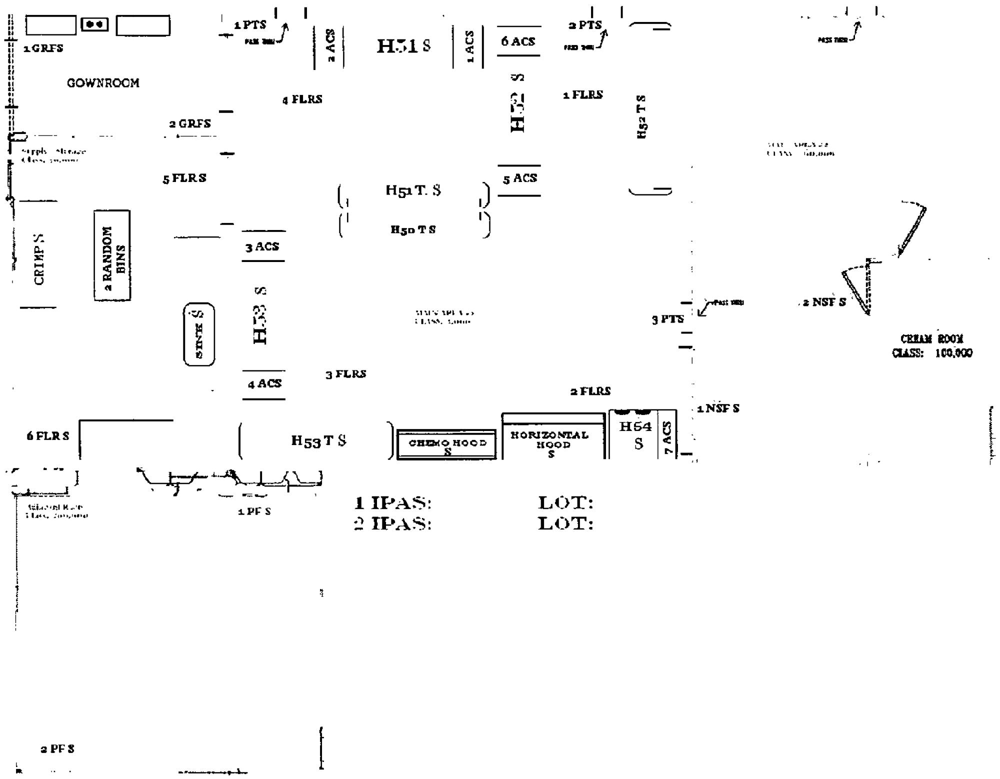

PASS THRU
H51 A
PASS THRU
PASS THRU
GOWNROOM A
H52 A
H52 TA
H51 TA
NS BENCH
A
CRIMP A
SINK A
H53 A
MIDDLE ROOM A
PASS THRU
CREAM ROOM
CLASS: 100,000
NRNS A
H53 TA
CHEMO HOOD
A
HORIZONTAL
HOOD
A
H54
A
1 PREP A
2 PREP A

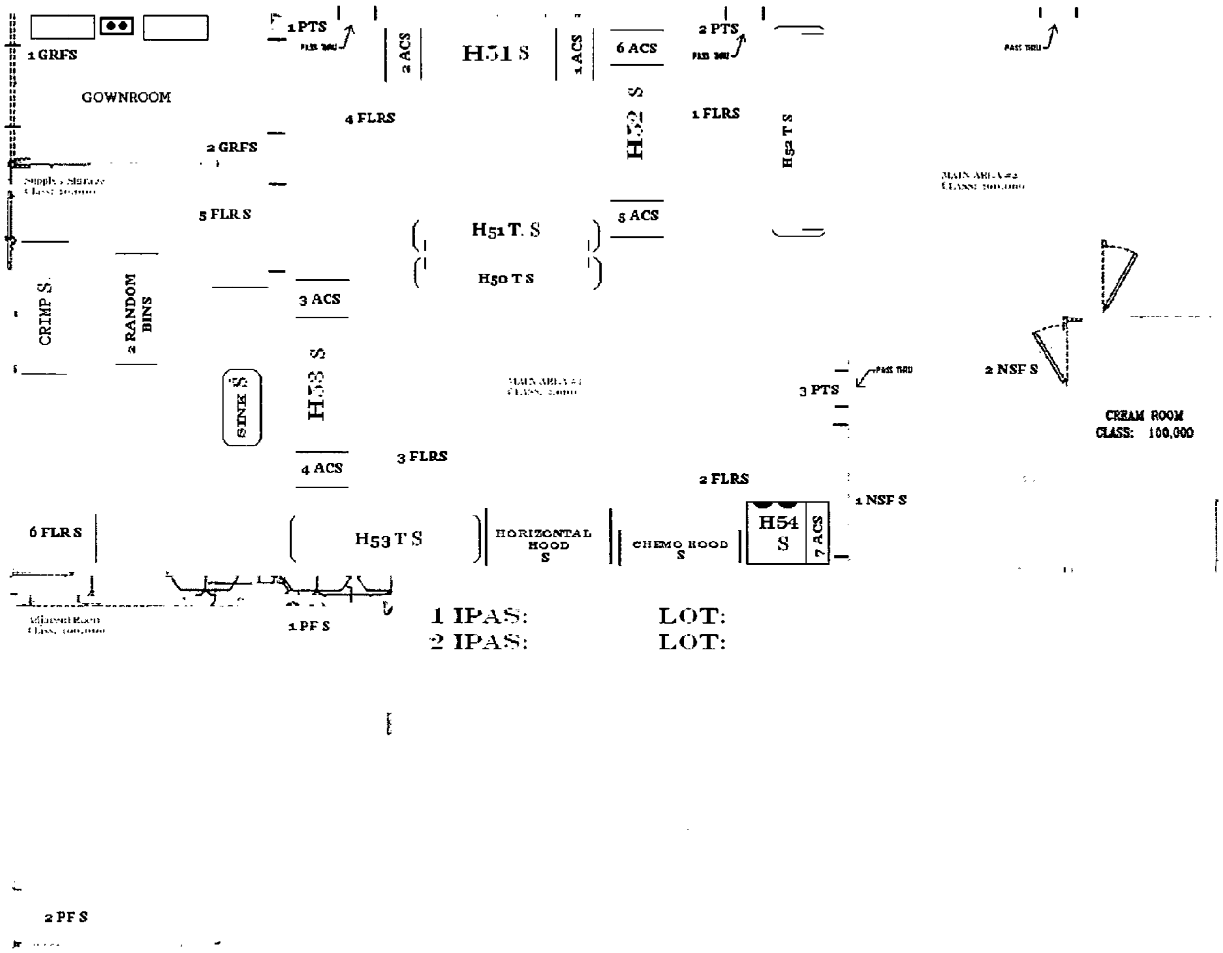
Clean Room Viable Air Sampling Diagram



Clean Room Surface Sampling Diagram



1 IPAS: LOT:
2 IPAS: LOT:



1 IPAS:　　LOT:
2 IPAS:　　LOT:

TITLE: ENVIRONMENTAL MONITORING OF THE CLEAN ROOM FACILITY

SOP NUMBER: 3.030 VERSION NUMBER: 4.0

CLEAN ROOM VIABLE AIR SAMPLING - ATTACHMENT 6

Page 1 of 1

Sample Location	Description	Results			Alert/Action
		Bacteria CFU	*Mold CFU*	*Total CFU*	
H51A	Hood 1				☐Al ☐Ac
H52A	Hood 2				☐Al ☐Ac
H53A	Hood 3				☐Al ☐Ac
H54A	Hood 4				☐Al ☐Ac
H55A	Hood 5				☐Al ☐Ac
ChemoA	Chemo Hood				☐Al ☐Ac
HorizA	Horizontal Hood				☐Al ☐Ac
H51TA	Table 2				☐Al ☐Ac
H52TA	Table 3				☐Al ☐Ac
H53TA	Table 4				☐Al ☐Ac
GownroomA	Gowning Area				☐Al ☐Ac
SinkA	Sink Area				☐Al ☐Ac
CrimpA	Crimping Bench				☐Al ☐Ac
MiddleroomA	Middle of Room				☐Al ☐Ac
NRNSA	Near Non-Sterile Lab				☐Al ☐Ac
1PrepA	Prep Room – Near Incubator				☐Al ☐Ac
2PrepA	Prep Room – Near Warehouse				☐Al ☐Ac

Alert		**Action**
1 CFU	ISO 4 (class 10) Glove box, Antechambers	2+ CFU
2 CFU	ISO 6 (class 1,000) Main Clean room	4+ CFU
5 CFU	ISO 7 (class 10,000) Gown room, Crimp room	8+ CFU
8 CFU	ISO 8 (class 100,000) Prep room	10+ CFU

Date of Sampling: Media Lot: Exp Date:

Sampler Mfg/Model: Serial #: Calibration Due Date:

Quality Control: Date:

Reviewed By: Date:

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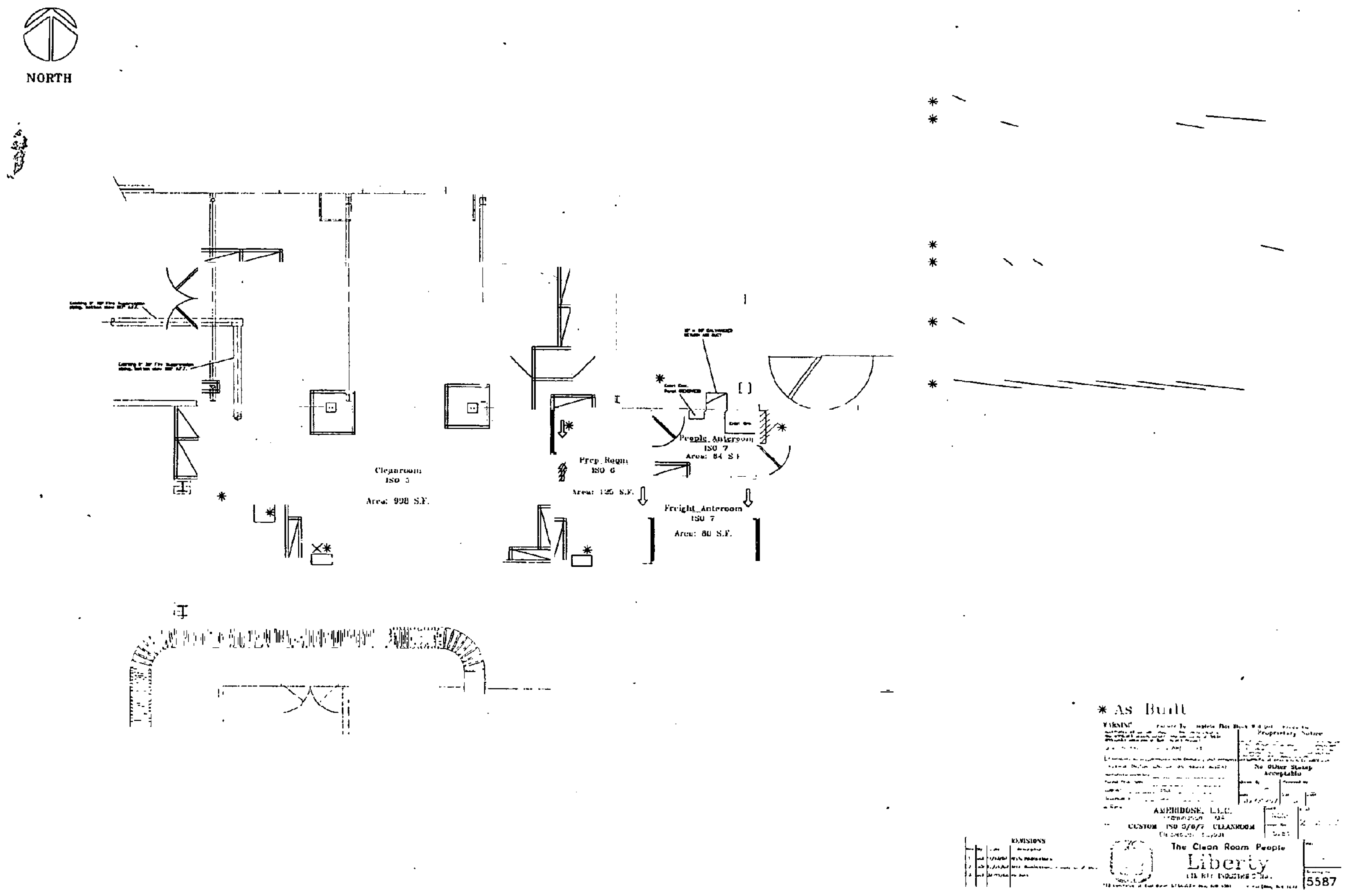
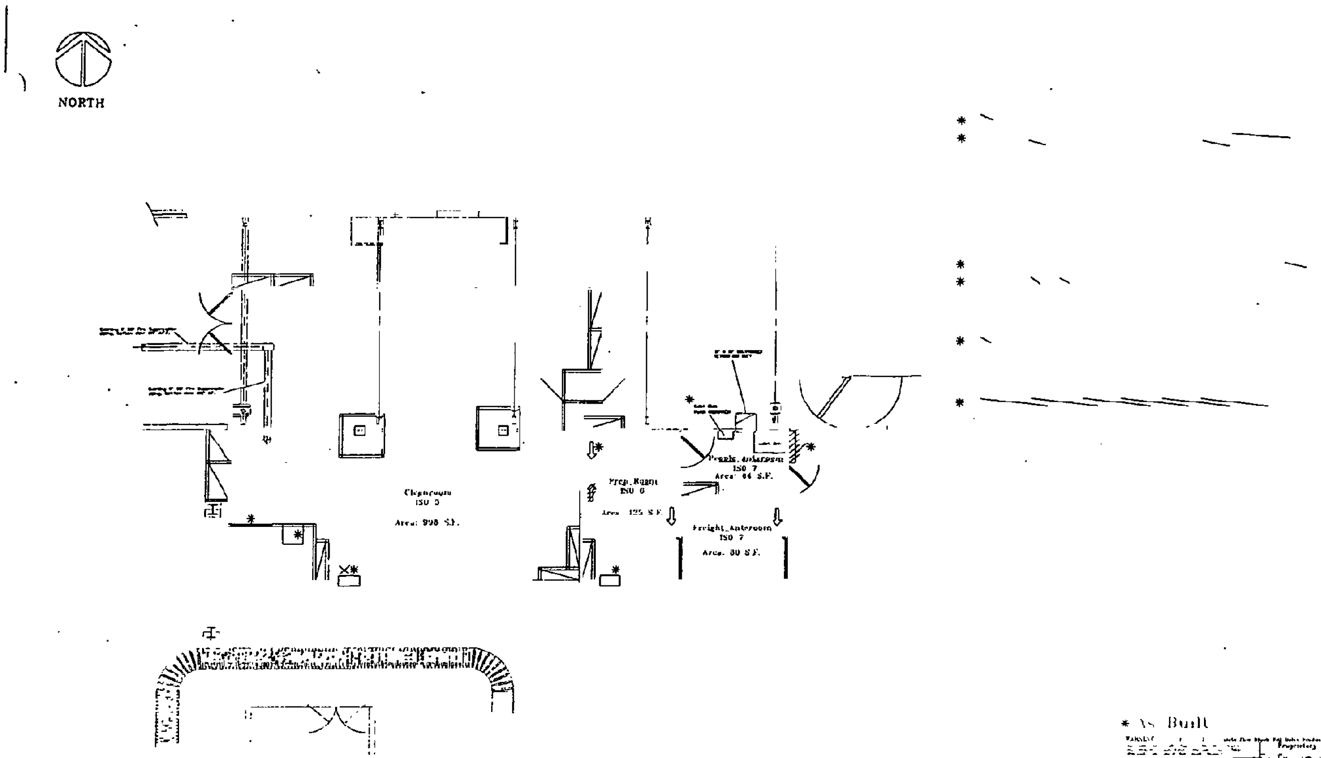
07-22-06

CLEAN ROOM
TWO

Diagram CKL


NORTH
Cleanroom
ISO 5
Area: 998 S.F.
Prep Room
ISO 6
Area: 125 S.F.
People Anteroom
ISO 7
Area: 84 S.F.
Freight Anteroom
ISO 7
Area: 80 S.F.
* As Built
WARNING
Proprietary Notice
No Other Stamp Acceptable
AMERIDOSE, L.L.C.
CUSTOM ISO 5/6/7 CLEANROOM
REVISIONS
The Clean Room People
Liberty
5587



* As Built

Proprietary Notice

REVISIONS

AMERIDOSE LLC

CUSTOM ISO 5/6/7 CLEANROOM

The Clean Room People

Liberty

LIBERTY INDUSTRIES, INC.

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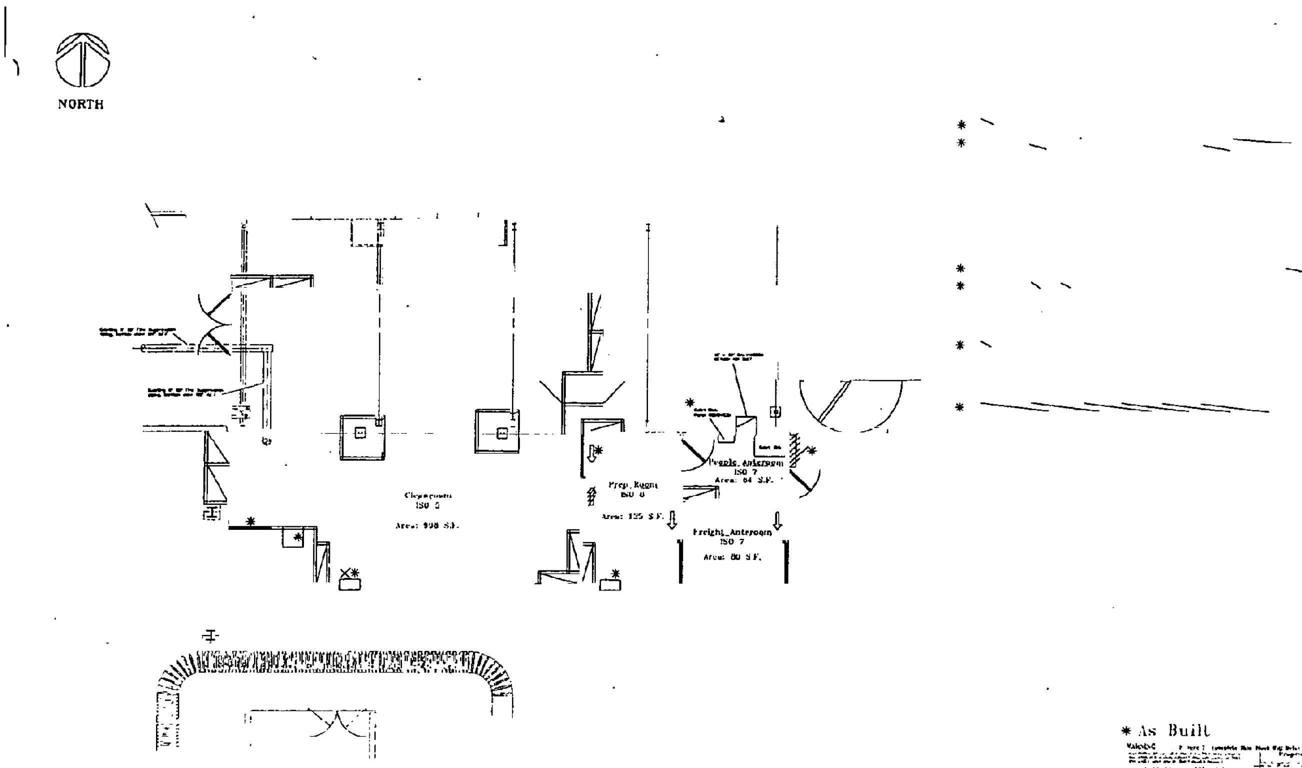

* As Built

Proprietary Notes

AMERIDOSE L.L.C.

CUSTOM ISO 5/7/8 CLEANROOM

REVISIONS

The Clean Room People

Liberty

LIBERTY INDUSTRIES, Inc.

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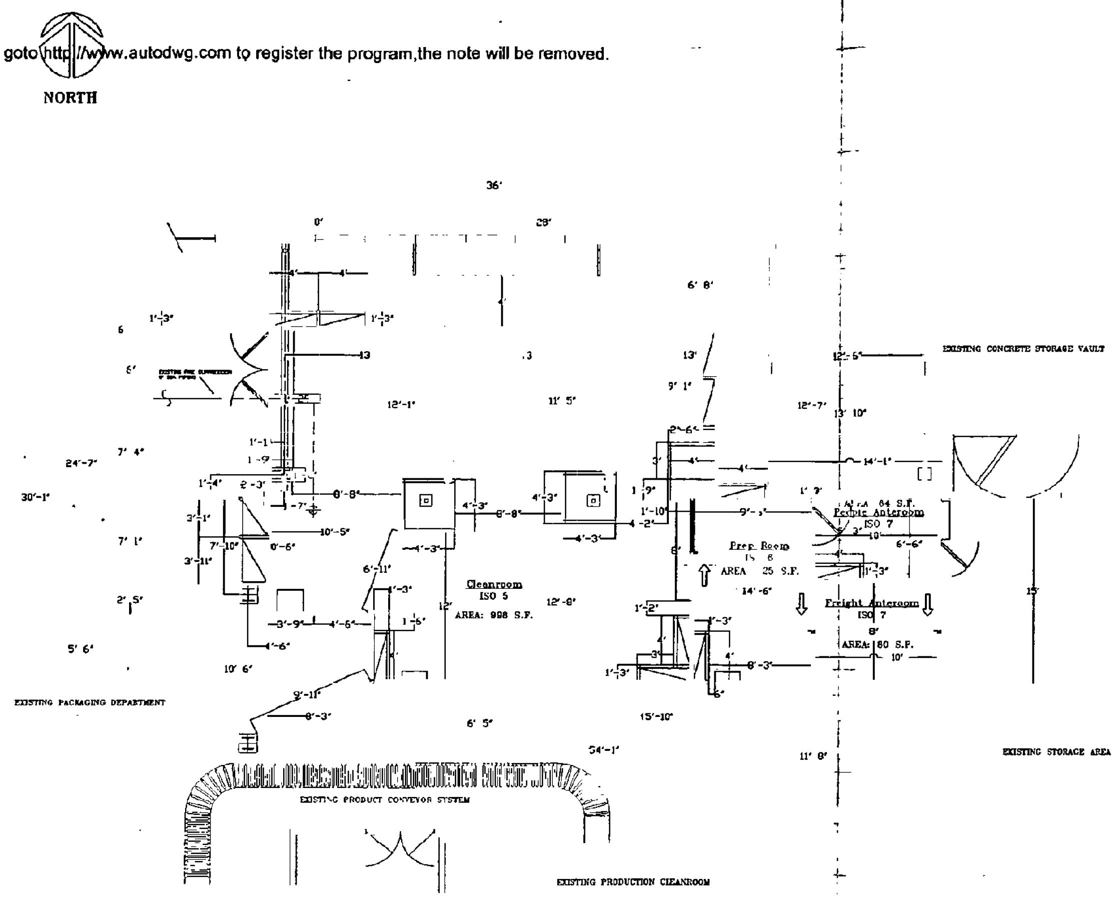
AutoDWG DWGSee Trial Version. http://www.autodwg.com

Please goto http://www.autodwg.com to register the program,the note will be removed.



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WARNING Failure To Complete This Block Will Delay Production

[illegible]

☐ [illegible] ☐ [illegible] ☐ [illegible]

PLEASE INITIAL ONE OF THE ABOVE BLOCKS

Proprietary Notice

No Other Stamp Acceptable

Drawn By JCC	Reviewed By	
Date 09/21/07	Size D	Date

Job Name AMERIDOSE L.L.C.
Framingham MA.

Title CUSTOM ISO 5/6/7 CLEANROOM
Cleanroom Dimensions

Scale NONE
Model No. 5283
Sheet 4 of 16

The Clean Room People
Liberty
LIBERTY INDUSTRIES INC.

Rev 1
Drawing No. 5587

REVISIONS